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A 24-year-old man comes to the emergency department due to a painful erection for the past 6 hours. He has never had this condition before and says it is unrelated to sexual excitement. Medical history is significant for treatment-resistant major depressive disorder, obsessive-compulsive disorder, and insomnia. The patient has smoked a pack of cigarettes a day for 2 years and drinks 1 or 2 cans of beer daily. Examination reveals engorged corpora cavernosa but otherwise shows no abnormalities. Which of the following drugs is the most likely cause of this patient's condition?

A. Bupropion
B. Citalopram
C. Clomipramine
D. Imipramine
E. Paroxetine
F. Phenelzine
G. Trazodone
H. Zolpidem

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H. Zolpidem

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The patient has smoked a pack of cigarettes a day for 2 years and drinks 1 or 2 cans of beer daily. Examination reveals engorged corpora cavernosa but otherwise shows no abnormalities. Which of the following drugs is the most likely cause of this patient's condition?

- A. Bupropion (7%)
- B. Citalopram (2%)
- C. Clomipramine (1%)
- D. Imipramine (2%)
- E. Paroxetine (3%)
- F. Phenelzine (4%)
- ✓ G. Trazodone (76%)
- H. Zolpidem (1%)

Correct

76%
Answered correctly

01 min, 20 secs
Time Spent

02/15/2021
Last Updated

Trazodone is a **sedating antidepressant** used off-label most often as a hypnotic to treat **insomnia** associated with depression or antidepressant treatment. It has been associated with the rare but serious side effect of **priapism** (ie, persistent erection of the penis for >4 hours that is not associated with sexual excitement). Priapism is a medical emergency that, if left untreated, can result in permanent damage to penile tissue and erectile dysfunction. Priapism occurs most often in young adult men.

Trazodone is a serotonin modulator (it antagonizes postsynaptic serotonin receptors and inhibits serotonin reuptake) that has minimal effects on norepinephrine and dopamine. Additional properties include alpha-adrenergic blockade—which may account for the side effects of orthostatic hypotension and priapism—and histamine H1 receptor antagonism, which contributes to its sedating effect. Trazodone should be used with caution in patients with conditions that predispose to priapism (eg, **sickle cell disease**).

(Choices A, B, and E) These antidepressants have not been associated with priapism. Bupropion is a dopamine-norepinephrine reuptake inhibitor that is not associated with sexual side effects and may reduce sexual side effects induced by selective serotonin reuptake inhibitors (SSRIs) when used as an adjunctive treatment. Citalopram and paroxetine, in contrast, are SSRIs that have been associated with high rates of sexual side effects (eg, decreased libido, anorgasmia, delayed ejaculation).

(Choices C, D, and F) Clomipramine and imipramine are tricyclic antidepressants used as second-line

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(Choices C, D, and F) Clomipramine and imipramine are tricyclic antidepressants used as second-line therapy due to their higher side effect burden and risk for cardiotoxicity in overdose. Phenelzine is a monoamine oxidase inhibitor used in the treatment of resistant depression; it requires dietary restrictions due to the risk of hypertensive crisis. These agents do not typically cause priapism.

(Choice H) Zolpidem is a nonbenzodiazepine hypnotic used in the treatment of insomnia; it does not carry a risk of priapism.

Educational objective:
Trazodone is a highly sedating antidepressant commonly used to treat insomnia. Priapism is a rare but serious adverse effect.

References

- Off-label trazodone prescription: evidence, benefits and risks.
- Trazodone for insomnia: a systematic review.

Pharmacology Male Reproductive System Priapism

A 35-year-old man comes to the office due to a lack of sexual interest. He says, "I started seeing this woman 9 months ago and am really attracted to her. We get along well and things are great, but I just don't want to have sex with her anymore." On further questioning, the patient reluctantly admits that whenever they have intercourse he has an orgasm in less than a minute and finds this very embarrassing. He does not have the same problem when he masturbates. He says, "I'm worried that my girlfriend will leave me, and it's really affecting my self-esteem." The patient has no other concerns. His other medical conditions include type 1 diabetes mellitus, chronic insomnia, and a history of major depression. His medications include insulin glargine, short-acting insulin, and trazodone. He does not use illicit substances. Vital signs are within normal limits. Laboratory results are significant for hemoglobin A1c of 7% and fasting glucose of 130 mg/dL. Which of the following is the most likely diagnosis?

A. Erectile disorder
B. Male hypoactive sexual desire disorder
C. Premature ejaculation
D. Sexual dysfunction due to diabetes
E. Sexual dysfunction due to major depressive disorder

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A. Erectile disorder
B. Male hypoactive sexual desire disorder
C. Premature ejaculation
D. Sexual dysfunction due to diabetes
E. Sexual dysfunction due to major depressive disorder
F. Substance/medication-induced sexual dysfunction

Submit

they have intercourse he has an orgasm in less than a minute and finds this very embarrassing. He does not have the same problem when he masturbates. He says, "I'm worried that my girlfriend will leave me, and it's really affecting my self-esteem." The patient has no other concerns. His other medical conditions include type 1 diabetes mellitus, chronic insomnia, and a history of major depression. His medications include insulin glargine, short-acting insulin, and trazodone. He does not use illicit substances. Vital signs are within normal limits. Laboratory results are significant for hemoglobin A1c of 7% and fasting glucose of 130 mg/dL. Which of the following is the most likely diagnosis?

- A. Erectile disorder (1%)
- B. Male hypoactive sexual desire disorder (2%)
- ✓ C. Premature ejaculation (66%)
- D. Sexual dysfunction due to diabetes (3%)
- E. Sexual dysfunction due to major depressive disorder (4%)
- F. Substance/medication-induced sexual dysfunction (21%)

Evaluation of sexual dysfunction requires ruling out medical conditions and substance use, as well as obtaining a history of psychosocial stressors, including stressors in the relationship itself. This patient has features of **premature ejaculation**, characterized by unwanted episodes of early ejaculation accompanied by a sense of lack of control. Although concern over the time to ejaculation is common, only an estimated 4% of men will meet diagnostic criteria (ejaculation **within one minute** of penetration, occurring most of the time **for at least 6 months**). The diagnostic criteria for premature ejaculation are based on ejaculation during partnered sexual activity, therefore a normal time to ejaculation during masturbation does not negate this diagnosis.

(Choice A) Erectile disorder is characterized by a persistent inability to attain or sustain an erection.

(Choice B) The symptom reported initially was a lack of sexual interest. However, on further questioning, it was found to be related to his embarrassment over premature ejaculation rather than to a pervasive lack of desire. It is common for men with premature ejaculation to develop anxiety and resultant aversion to sexual intercourse.

(Choice D) Medical conditions, including diabetes, that affect nerve function or blood flow to the pelvic tissue tend to result in erectile dysfunction rather than premature ejaculation. Medical conditions linked to

of desire. It is common for men with premature ejaculation to develop anxiety and resultant aversion to sexual intercourse.

(Choice D) Medical conditions, including diabetes, that affect nerve function or blood flow to the pelvic tissue tend to result in erectile dysfunction rather than premature ejaculation. Medical conditions linked to premature ejaculation include prostatitis and thyroid disease.

(Choice E) Sexual dysfunction may occur in the context of psychiatric conditions, such as depression and anxiety. Apart from the distress secondary to his ejaculatory disorder, this patient reports no depressive symptoms.

(Choice F) Trazodone is a serotonin modulator used primarily for the treatment of insomnia. It may cause priapism (ie, persistent erection), but it does not cause premature ejaculation (nor does insulin).

Educational objective:
Premature ejaculation is characterized by recurrent episodes of early ejaculation accompanied by a sense of lack of control. Evaluation of any sexual disorder requires taking careful medical and substance use histories and assessing psychosocial stressors and comorbid psychiatric conditions.

References

A 25-year-old Caucasian man is undergoing evaluation for azoospermia. The patient has been monogamous with his long-term girlfriend and does not use contraception during sexual intercourse. They have been trying to conceive for the past year with no success. The patient has a past medical history of recurrent pneumonia with frequent hospitalizations for antibiotic treatment. He takes no medications and does not use tobacco, alcohol, or illicit drugs. The patient has no allergies and his immunizations are up-to-date. His family history is unknown as he was adopted as an infant. Physical examination shows digital clubbing. A transrectal ultrasound shows bilateral absence of the vas deferens. Which of the following tests would most likely confirm the underlying diagnosis of this patient's condition?

A. Chloride level in the sweat
B. Cilia motility of the nasal epithelium
C. Serum alpha-1 antitrypsin level
D. Serum FSH and LH levels
E. Serum IgA levels
F. Serum testosterone levels

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- A. Chloride level in the sweat (62%)
- B. Cilia motility of the nasal epithelium (26%)
- C. Serum alpha-1 antitrypsin level (1%)
- D. Serum FSH and LH levels (3%)
- E. Serum IgA levels (0%)
- F. Serum testosterone levels (4%)

Primary ciliary dyskinesia versus cystic fibrosis

	Primary ciliary dyskinesia	Cystic fibrosis
Pathogenesis	• **Dynein arm defect** → abnormal ciliary motion & impaired mucociliary clearance	• Mutation in the ***CFTR* gene** → impaired ion transport
Respiratory tract features	• Chronic sinopulmonary infections • Nasal polyps • Bronchiectasis • Digital clubbing	• Chronic sinopulmonary infections • Nasal polyps • Bronchiectasis • Digital clubbing
Extrapulmonary features	• Situs inversus (50% of cases) • Infertility due to immotile spermatozoa • Normal growth	• Pancreatic insufficiency • Infertility due to absent vas deferens (azoospermia) • Failure to thrive
Diagnosis	• Low nasal nitric oxide levels • Bronchoscopy & electron microscopic visualization of	• Elevated sweat chloride levels • Abnormal nasal transepithelial potential difference

Diagnosis	• Low nasal nitric oxide levels • Bronchoscopy & electron microscopic visualization of ciliary abnormalities • Genetic testing	• Elevated sweat chloride levels • Abnormal nasal transepithelial potential difference • Genetic testing

This patient has a history of recurrent pneumonia, digital clubbing, azoospermia, and bilateral absence of the vas deferens; this is most likely due to **cystic fibrosis (CF)**. Patients with CF have variable severity of lung and pancreatic function. Although most patients have recurrent sinopulmonary infections and pancreatic insufficiency, some patients may have mild disease depending on their underlying mutation. Regardless of lung or pancreas function, virtually all adult men with CF have **azoospermia** and **infertility**. Although spermatogenesis is usually normal, almost all males with CF are unable to secrete semen due to **congenital bilateral absence of the vas deferens (CBAVD)**. ***CFTR* mutations** are likely responsible for abnormal development of Wolffian structures, resulting in vasal agenesis and defective sperm transport.

A diagnosis of CF can be based on **elevated sweat chloride levels**. If the sweat chloride test is equivocal, measurement of **nasal transepithelial potential difference** and genetic testing for *CFTR* mutations should be performed to confirm the diagnosis.

(Choice B) Although, primary ciliary dyskinesia (eg, Kartagener syndrome) can cause recurrent pulmonary infections and digital clubbing, infertility in Kartagener syndrome is usually due to immotile spermatozoa. Abnormal nasociliary motility is a nonspecific finding that is seen most commonly in patients with primary ciliary dyskinesia and in some patients with CF (due to abnormally thick mucus). A more specific test for CF is the nasal transepithelial potential difference. In addition, CBAVD is virtually pathognomonic for a *CFTR* mutation.

(Choice C) Low serum alpha-1 antitrypsin (AAT) is associated with AAT deficiency and not with CF. AAT deficiency is typically associated with panacinar emphysema and chronic liver disease. Infertility is not seen in these patients.

(Choices D and F) FSH, LH, and testosterone levels are usually normal in patients with CF. A low testosterone level in the setting of decreased FSH and LH is seen in hypogonadotropic hypogonadism (eg, Kallmann syndrome).

(Choice E) Primary humoral deficiencies usually manifest as recurrent upper and lower respiratory tract infections due to impaired antibody production. However, most patients with selective IgA deficiency are asymptomatic.

Educational objective:

(Choice C) Low serum alpha-1 antitrypsin (AAT) is associated with AAT deficiency and not with CF. AAT deficiency is typically associated with panacinar emphysema and chronic liver disease. Infertility is not seen in these patients.

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(Choice E) Primary humoral deficiencies usually manifest as recurrent upper and lower respiratory tract infections due to impaired antibody production. However, most patients with selective IgA deficiency are asymptomatic.

Educational objective:

CFTR gene mutations are the most common cause of congenital bilateral absence of the vas deferens (CBAVD). Patients with CBAVD have azoospermia and infertility but normal levels of FSH, LH, and testosterone. Elevated sweat chloride levels are diagnostic of cystic fibrosis.

References

- Management of male infertility due to congenital bilateral absence of vas deferens should not ignore the

A 19-year-old man comes to the emergency department due to intense scrotal pain over the past 6 hours. The pain started shortly after participating in a soccer game; he does not recall any specific trauma. The patient took ibuprofen at home with minimal relief. He is sexually active and has been treated twice in the past for *Neisseria gonorrhoeae*. Temperature is 36.9 C (98.5 F), blood pressure is 110/86 mm Hg, and pulse is 92/min. On examination, there is no inguinal adenopathy. There is significant discomfort with scrotal examination primarily on the right where a high-riding swollen mass is palpated within the hemiscrotum. The left testicle is palpated lower in the scrotum. Which of the following additional physical examination findings is most likely present in this patient?

A. Absent elevation of the right testicle with stroking of the ipsilateral thigh
B. Enlargement of the mass when the patient coughs or bears down
C. Increase in the size of the mass when standing relative to laying
D. Reduction in pain with manual elevation of the right testicle
E. Transillumination of the mass when a flashlight is placed behind the scrotum

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- A. Absent elevation of the right testicle with stroking of the ipsilateral thigh (65%)
- B. Enlargement of the mass when the patient coughs or bears down (7%)
- C. Increase in the size of the mass when standing relative to laying (3%)
- D. Reduction in pain with manual elevation of the right testicle (17%)
- E. Transillumination of the mass when a flashlight is placed behind the scrotum (6%)

Correct

65%

01 min, 18 secs

09/18/2020

Testicular torsion	
Pathogenesis	• Twisting of spermatic cord • Venous congestion, hemorrhagic infarction & necrosis of testis • ↑ Risk with poor fixation of testis to tunica vaginalis
Clinical features	• Testicular, inguinal, or abdominal pain • Nausea, vomiting • Examination findings ◦ Swollen, erythematous hemiscrotum ◦ Elevated, horizontally positioned testicle ◦ Absent cremasteric reflex
Imaging	• No testicular blood flow on Doppler ultrasound
Management	• Immediate surgical detorsion

This patient has acute, severe, progressive scrotal pain with a high-riding scrotal mass, findings concerning for **testicular torsion**. Torsion is caused by twisting of the spermatic cord and its contents, leading to

This patient has acute, severe, progressive scrotal pain with a high-riding scrotal mass, findings concerning for **testicular torsion**. Torsion is caused by twisting of the spermatic cord and its contents, leading to venous congestion, ischemia, and necrosis of the testis if untreated.

Classic presentation is an adolescent or young adult male with **sudden onset** of **unilateral scrotal pain**, usually with associated nausea and vomiting. Poor testicular perfusion can also cause reactive **scrotal edema** and **discoloration** (eg, erythema) on examination. Because the cremaster muscle lies within the spermatic cord, an **absent cremasteric reflex** (testicular elevation when stroking the ipsilateral inner thigh) is highly suggestive of testicular torsion. The testicle itself is often transverse (due to inadequate fixation of the lower pole of the testis to the tunica vaginalis) and **high riding** (due to cord shortening with rotation).

Diagnosis can be clinical with classic findings or may require ultrasound evaluation. Twisting of the spermatic cord and/or decreased testicular perfusion on ultrasound confirms the diagnosis.

(Choice B) Increased abdominal pressure (eg, cough, Valsalva maneuver) can lead to bulging within the groin or scrotum due to an inguinal hernia. If incarcerated, a hernia can lead to acute scrotal pain, but a high-riding testicle would not be expected.

(Choice C) Varicocele, which is characterized by a scrotal mass with a "bag of worms" texture, increases in size when standing as compared with supine positioning. This dilation of the pampiniform plexus may

high-riding testicle would not be expected.

(Choice C) Varicocele, which is characterized by a scrotal mass with a "bag of worms" texture, increases in size when standing as compared with supine positioning. This dilation of the pampiniform plexus may cause a dull ache, but not acute, severe pain.

(Choice D) Epididymitis caused by infection (eg, *Neisseria gonorrhoeae*) or trauma causes acute scrotal pain that is relieved with manual elevation of the testicle. In contrast to this case, urinary symptoms (eg, dysuria, frequency, urgency) are typical, and a high-riding testicle would not be seen.

(Choice E) Hydrocele is a fluid collection within the tunica vaginalis that transilluminates on examination and causes scrotal enlargement but not acute pain.

Educational objective:

Testicular torsion presents with acute, severe, progressive unilateral scrotal pain. Classic examination findings include scrotal edema and discoloration, a high-riding testicle, and an absent cremasteric reflex (ie, absence of testicular elevation when stroking the ipsilateral thigh).

References

- Cremasteric reflex.

A 17-year-old boy comes to the office for evaluation of gynecomastia. Examination shows sparse facial and pubic hair. Laboratory studies show:

Serum testosterone	high
Serum LH	high
Serum FSH	normal

Semen analysis reveals severe oligospermia. Which of the following mechanisms is the most likely cause of this patient's condition?

A. Androgen receptor dysfunction
B. Damage to seminiferous tubules
C. Ejaculatory duct obstruction
D. Exogenous androgen use
E. Impaired Leydig cell function

and public hair. Laboratory studies show:

Serum testosterone	high
Serum LH	high
Serum FSH	normal

Semen analysis reveals severe oligospermia. Which of the following mechanisms is the most likely cause of this patient's condition?

- A. Androgen receptor dysfunction (75%)
- B. Damage to seminiferous tubules (6%)
- C. Ejaculatory duct obstruction (0%)
- D. Exogenous androgen use (11%)
- E. Impaired Leydig cell function (5%)

Correct

75%

01 min, 48 secs

11/05/2020

Hormonal changes in oligospermia	
Ejaculatory duct obstruction	• Normal FSH, LH, testosterone
Primary hypogonadism	• Low testosterone • Elevated FSH, LH
Secondary (hypogonadotropic) hypogonadism	• Low testosterone • Low/normal FSH, LH
Partial androgen resistance	• Elevated LH, testosterone • Normal FSH

This patient has an **elevated testosterone** level, but his gynecomastia and sparse facial and pubic hair suggests lack of the expected physiologic response. **Androgen insensitivity syndrome (AIS)** is caused by **loss-of-function** mutations of the **androgen receptor** (AR) gene on the X chromosome. Complete AIS is characterized by female body habitus and external genitalia (but with absence of internal Mullerian derivatives) and cryptorchid testes. In contrast, **partial AIS** has a variable phenotype; typical findings include:

- **Undervirilization** of the external genitalia, ranging from phenotypically female to phenotypically male (often with microphallus and hypospadias)
- Decreased facial, axillary, and pubic hair (which is driven by androgens in both males and females)
- **Oligospermia**
- **Gynecomastia**

Dysfunction of the AR in the hypothalamus and pituitary leads to loss of feedback inhibition of gonadotropin-releasing hormone (GnRH), FSH, and LH. This results in the following hormonal findings:

- GnRH induces **increased LH secretion**, which leads to **increased testosterone production** in the testes.
- FSH secretion is increased by GnRH but suppressed by inhibin from the seminiferous tubules and is often normal.
- Estrogen, which is derived by aromatization of testosterone, may be normal or elevated.

(Choices B and E) Testicular disorders can affect the Leydig cells, seminiferous tubules, or both. The Leydig cells are the primary site of testosterone production; reduced Leydig cell function can cause

(Choices B and E) Testicular disorders can affect the Leydig cells, seminiferous tubules, or both. The Leydig cells are the primary site of testosterone production; reduced Leydig cell function can cause gynecomastia and elevated LH but would be associated with low (not high) testosterone. Injury to the seminiferous tubules leads to loss of inhibin feedback of FSH secretion and an elevated FSH.

(Choice C) Ejaculatory duct obstruction can be caused by congenital defects or infection (eg, *Chlamydia trachomatis*). Sperm counts are low but testicular endocrine function (ie, testosterone level) is typically normal.

(Choice D) Abuse of exogenous androgens can reduce spermatogenesis (due to reduced local testicular testosterone levels) and cause gynecomastia (due to aromatization of excess androgens to estrogens). However, this would be associated with suppression of LH levels.

Educational objective:
Androgen receptor dysfunction in patients with partial androgen insensitivity syndrome leads to decreased facial, axillary, and pubic hair; oligospermia; gynecomastia; and undervirilization of external genitalia (eg, microphallus). Loss of feedback inhibition of gonadotropin-releasing hormone results in elevated LH and testosterone levels.

A 78-year-old man comes to the office for a regularly scheduled review of his chronic medical problems. The patient has hypertension, coronary artery disease, and type 2 diabetes mellitus, for which he takes metformin, atorvastatin, lisinopril, and nitroglycerin as needed for chest pain. He takes his medications as prescribed and follows diet and exercise instructions. During the discussion, he hesitates, laughs nervously, and says, "I can't get an erection anymore, and my wife says I have to ask you about getting the 'blue pill.'" Which of the following is the most appropriate response to this patient's concern?

A. "I can see that you feel uncomfortable talking about this. It can be a sensitive subject for some men."

B. "I can understand your concern, but at your age, we hesitate to start too many medications."

C. "Medications for erectile dysfunction have significant side effects. I would not pursue them unless you feel it is important."

D. "This is a very common problem for men as they age. It is good that you mentioned it."

E. "We can try medication for erectile dysfunction, but it may not be effective at your age."

A 70-year-old man comes to the office for a regularly scheduled review of his chronic medical problems. The patient has hypertension, coronary artery disease, and type 2 diabetes mellitus, for which he takes metformin, atorvastatin, lisinopril, and nitroglycerin as needed for chest pain. He takes his medications as prescribed and follows diet and exercise instructions. During the discussion, he hesitates, laughs nervously, and says, "I can't get an erection anymore, and my wife says I have to ask you about getting the 'blue pill.'" Which of the following is the most appropriate response to this patient's concern?

A. "I can see that you feel uncomfortable talking about this. It can be a sensitive subject for some men." (18%)

B. "I can understand your concern, but at your age, we hesitate to start too many medications." (2%)

C. "Medications for erectile dysfunction have significant side effects. I would not pursue them unless you feel it is important." (5%)

✓ D. "This is a very common problem for men as they age. It is good that you mentioned it." (73%)

E. "We can try medication for erectile dysfunction, but it may not be effective at your age." (0%)

Discussing sexuality with older patients	
Empathy & reassurance	• Sexuality is a normal & appropriate topic of discussion at any age. • Sexual problems are common in the elderly. • Clinician is willing to work with the patient as appropriate.
Patient-centered education	• Allow the patient to set priorities & subject boundaries. • Use appropriate vocabulary (avoid medical jargon & euphemisms). • Be aware of comorbidities & concurrent medications.

Sexual dysfunction is common in older individuals due to comorbid conditions, medication effects, and in women, menopausal changes. This patient is experiencing difficulty with sexual intercourse, and his hesitation in discussing it suggests that he feels awkward in bringing up the subject.

In counseling a patient on a potentially **sensitive subject** such as sexuality, the first objective is **making the patient feel comfortable**. The clinician should discuss the topic objectively, as with any other medical topic, and avoid giving the impression that the subject of sex is "dirty" or inappropriate. It is generally best to use the same terms the patient uses for bodily functions but otherwise avoid euphemisms. In this

the patient feel comfortable. The clinician should discuss the topic objectively, as with any other medical topic, and avoid giving the impression that the subject of sex is "dirty" or inappropriate. It is generally best to use the same terms the patient uses for bodily functions but otherwise avoid euphemisms. In this particular case, the clinician should begin the conversation by reassuring the patient that sexual dysfunction is **common** and is a perfectly **appropriate subject of discussion** between a patient and a physician.

(Choice A) The patient already appears to feel nervous discussing the subject of sexuality. This statement conveys empathy but reiterates and draws attention to his anxiety and may reinforce his feelings of awkwardness.

(Choices B and E) The patient takes a medication (ie, nitrates) that makes phosphodiesterase inhibitors (eg, sildenafil, sometimes referred to colloquially as "the blue pill") contraindicated. Although the use of phosphodiesterase inhibitors is often complicated in patients with cardiovascular disease, age itself is not a contraindication.

(Choice C) Patients are unlikely to bring up a sensitive subject, such as sexuality, if they do not consider it important. This statement may make the patient feel even more uncomfortable in having to justify raising the concern.

(Choices B and E) The patient takes a medication (ie, nitrates) that makes phosphodiesterase inhibitors (eg, sildenafil, sometimes referred to colloquially as "the blue pill") contraindicated. Although the use of phosphodiesterase inhibitors is often complicated in patients with cardiovascular disease, age itself is not a contraindication.

(Choice C) Patients are unlikely to bring up a sensitive subject, such as sexuality, if they do not consider it important. This statement may make the patient feel even more uncomfortable in having to justify raising the concern.

Educational objective:
Sexual dysfunction is common in older individuals due to comorbid conditions, medication effects, and in women, menopausal changes. When counseling patients on sexuality, the clinician should attempt to make them feel comfortable and reassure them that sexual dysfunction is common and is an appropriate subject of discussion between a patient and a physician.

Behavioral science	Male Reproductive System	Male sexual dysfunction
Subject	System	Topic

In normal female development, non-fusion of the urethral folds forms the labia minora and the vestibule of the vagina. In males, non-fusion of the urethral folds would most likely result in which of the following?

A. Bifid scrotum
B. Cryptorchidism
C. Epispadias
D. Hydrocele of the testis
E. Hypospadias

Submit

In normal female development, non-fusion of the urethral folds forms the labia minora and the vestibule of the vagina. In males, non-fusion of the urethral folds would most likely result in which of the following?

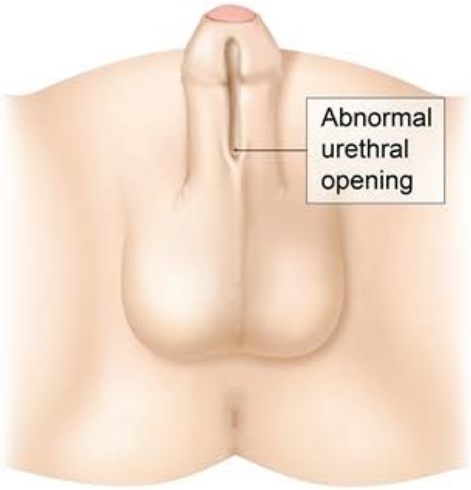
A. Bifid scrotum (9%)
B. Cryptorchidism (1%)
C. Epispadias (11%)
D. Hydrocele of the testis (1%)
✓ E. Hypospadias (77%)

Correct
77% Answered correctly
38 secs Time Spent
10/14/2020 Last Updated

Explanation

Hypospadias & epispadias

Hypospadias & epispadias



Hypospadias

Epispadias

Differentiation and development of the external genitalia occurs during **weeks 8-15** of gestation. In females, the urethral (urogenital) folds do not fuse and ultimately form the labia minora and the vestibule of the vagina. In males, the urethral folds fuse to form the ventral aspect of the penis and the penile raphe, which serve as the anterior wall of the urethra.

Differentiation and development of the external genitalia occurs during **weeks 8-15** of gestation. In females, the urethral (urogenital) folds do not fuse and ultimately form the labia minora and the vestibule of the vagina. In males, the urethral folds fuse to form the ventral aspect of the penis and the penile raphe, which serve as the anterior wall of the urethra.

Incomplete fusion of these folds in a male would result in an **abnormal opening** of the urethra at a location proximal to the distal tip of the glans penis. Depending on the degree of nonunion, the urethral opening can be anywhere from the perineum to just proximal to the glans penis. This condition is known as **hypospadias** and can generally be repaired surgically to allow normal urination and sexual activity.

(Choice A) A bifid scrotum (two separate sacs) results from malunion of the labioscrotal folds. In females, the labioscrotal swellings form the labia majora.

(Choice B) Cryptorchidism is failure of a fetal testis to descend into the scrotum. Most undescended testes will descend spontaneously by the time the infant is 4 months old.

(Choice C) The genital tubercle becomes the glans penis in males and the clitoris in females. Epispadias is an abnormal opening of the urethra on the dorsal surface of the penile shaft that results from faulty positioning of the genital tubercle in the fifth week of gestation.

(Choice D) The processus vaginalis is a projection of the peritoneal cavity that accompanies the

the labioscrotal swellings form the labia majora.

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(Choice D) The processus vaginalis is a projection of the peritoneal cavity that accompanies the descending testis into the scrotum and ultimately forms the tunica vaginalis of the testis. Hydrocele is development of a fluid-filled peritoneal sac within the scrotum that results from incomplete obliteration of the processus vaginalis.

Educational objective:
In males, incomplete fusion of the urethral (urogenital) folds results in hypospadias, an abnormal opening of the urethra proximal to the glans penis along the ventral shaft of the penis.

Embryology	Male Reproductive System	Hypospadia and epispadia
Subject	System	Topic

A 15-year-old patient is referred to the physician by a teacher who is concerned about the patient's learning abilities and behavior. The patient's reading and writing skills are significantly impaired compared to other classmates, and the patient often misbehaves in class despite receiving numerous detentions. Neuropsychological assessment shows mild intellectual disability. Cytogenetic studies show a karyotype containing 47 chromosomes. Which of the following findings are most likely to be present on further evaluation?

A. Arachnodactyly, scoliosis, aortic root dilation
B. Macroorchidism, large jaw and ears
C. Short stature, broad chest, amenorrhea
D. Short stature, hypotonia, obesity
E. Tall stature, gynecomastia, azoospermia

Submit

A 15-year-old patient is referred to the physician by a teacher who is concerned about the patient's learning abilities and behavior. The patient's reading and writing skills are significantly impaired compared to other classmates, and the patient often misbehaves in class despite receiving numerous detentions. Neuropsychological assessment shows mild intellectual disability. Cytogenetic studies show a karyotype containing 47 chromosomes. Which of the following findings are most likely to be present on further evaluation?

A. Arachnodactyly, scoliosis, aortic root dilation (2%)
B. Macroorchidism, large jaw and ears (15%)
C. Short stature, broad chest, amenorrhea (4%)
D. Short stature, hypotonia, obesity (6%)
✓ E. Tall stature, gynecomastia, azoospermia (70%)

Correct

70% Answered correctly

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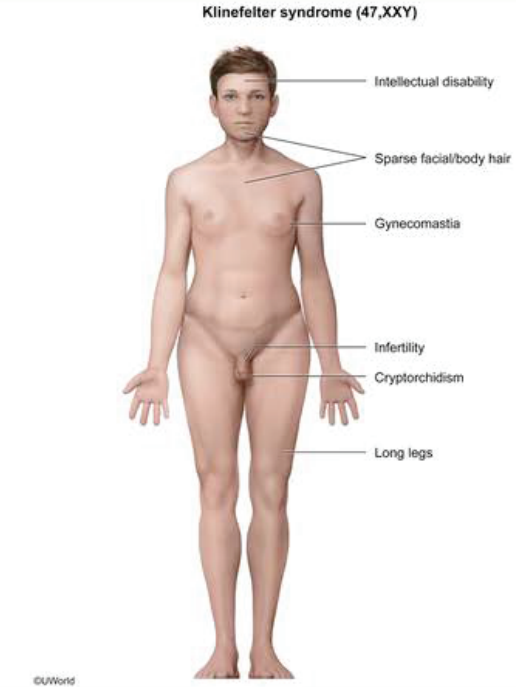

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Klinefelter syndrome is most commonly caused by a meiotic nondisjunction event during parental gametogenesis that results in a **47,XXY** karyotype. Variants include 46,XY/47,XXY mosaicism and 48,XXXY. In general, patients with higher numbers of X chromosomes are more likely to have more severe manifestations. The disorder is usually not diagnosed until puberty when the characteristic physical signs begin to develop. The major features are as follows:

1. Klinefelter syndrome causes **primary testicular failure** due to hyalinization and fibrosis of the seminiferous tubules. This results in small, firm testes and azoospermia (infertility). Leydig cell dysfunction also occurs and leads to testosterone deficiency. Gonadotropin (FSH, LH) levels are increased secondary to gonadal failure.
2. Testosterone deficiency results in development of a **eunuchoid body habitus**. Patients have tall stature and gynecomastia. Facial and body hair is sparse or absent and muscle mass is decreased.
3. Mild **intellectual disability** is seen in some patients, although the majority have normal intelligence. Psychosocial abnormalities (eg, lack of insight, poor judgment) are also common.

(Choice A) Arachnodactyly, scoliosis, and aortic root dilation are signs of Marfan syndrome, which occurs due to an inherited defect of the extracellular matrix protein fibrillin.

(Choice A) Arachnodactyly, scoliosis, and aortic root dilation are signs of Marfan syndrome, which occurs due to an inherited defect of the extracellular matrix protein fibrillin.

(Choice B) Macroorchidism, large jaw, and intellectual disability are seen in patients with fragile X syndrome, an X-linked disorder caused by mutations in the fragile X mental retardation 1 gene.

(Choice C) In females, loss of an X chromosome (45,XO karyotype) results in Turner syndrome, which presents with short stature, broad chest, and primary amenorrhea.

(Choice D) Prader-Willi syndrome is characterized by short stature, hypotonia, intellectual disability, and obesity. The most common cause is a microdeletion affecting the paternal chromosome 15q11-13 critical region.

Educational objective:
47,XXY is the most common genotype causing Klinefelter syndrome. Patients present with tall stature; small, firm testes; azoospermia; and gynecomastia. Mild intellectual disability is seen in some patients, and the severity generally increases with each additional X chromosome.

References

- The cognitive phenotype in Klinefelter syndrome: a review of the literature including genetic and hormonal factors

A 42-year-old man comes to the office seeking advice on male contraception. He and his wife have 6 healthy children and do not want any more. The patient's wife takes oral contraceptive pills but would like to stop due to weight gain. The patient's past medical history is notable for an appendectomy, during which he had no complications from the procedure or the associated anesthesia. He does not smoke. Examination shows a normal circumcised male with no visible genital lesions and no palpable abnormalities in the scrotum. After appropriate discussion regarding contraceptive options, the patient elects to undergo a vasectomy. Which of the following should the patient be advised to expect during the first month following the procedure?

A. Decreased interest in sexual activity
B. Difficulty in maintaining an erection
C. Large reduction in the volume of ejaculate
D. Reduced testosterone production
E. Viable sperm in the ejaculate

healthy children and do not want any more. The patient's wife takes oral contraceptive pills but would like to stop due to weight gain. The patient's past medical history is notable for an appendectomy, during which he had no complications from the procedure or the associated anesthesia. He does not smoke. Examination shows a normal circumcised male with no visible genital lesions and no palpable abnormalities in the scrotum. After appropriate discussion regarding contraceptive options, the patient elects to undergo a vasectomy. Which of the following should the patient be advised to expect during the first month following the procedure?

A. Decreased interest in sexual activity (1%)

B. Difficulty in maintaining an erection (4%)

C. Large reduction in the volume of ejaculate (16%)

D. Reduced testosterone production (1%)

✓ E. Viable sperm in the ejaculate (76%)

Correct

76%
Answered correctly

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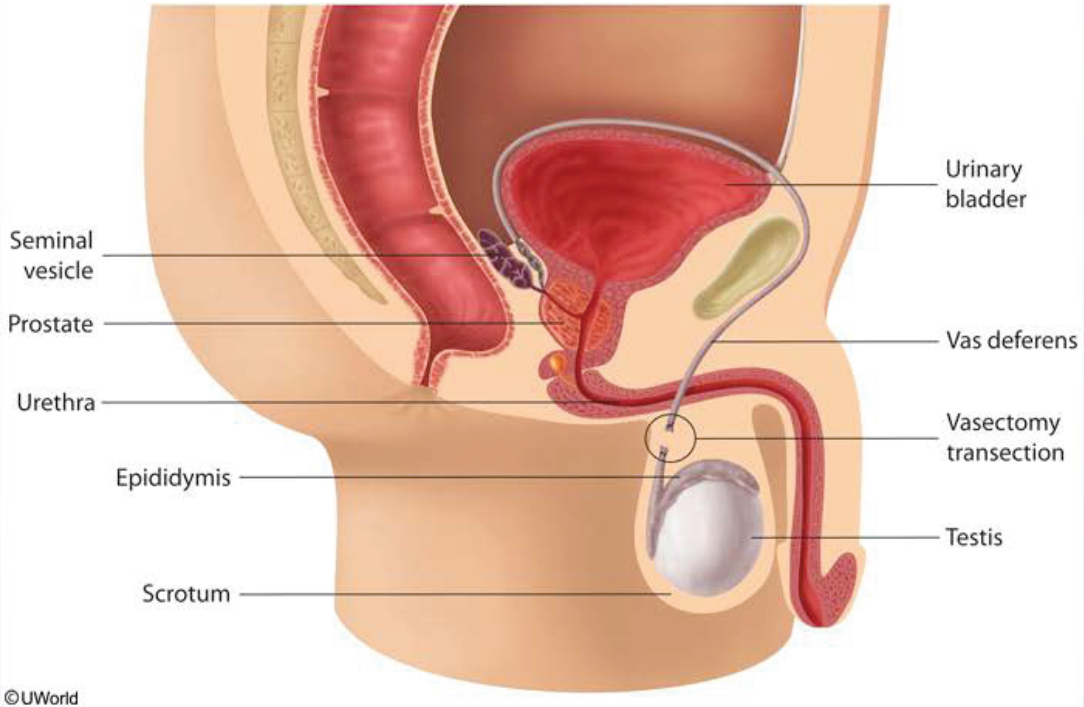
Vasectomy



Vasectomy involves transection of the **vas deferens**. The vas deferens functions not only as a transport

Vasectomy involves transection of the **vas deferens**. The vas deferens functions not only as a transport duct from the epididymis to the ejaculatory duct but also serves to store and protect sperm following spermatogenesis.

Vasectomy blocks the transport of new sperm from the epididymis but has no effect on sperm distal to the ligation. Patients can still have **viable sperm** in the distal vas for 3 months and at least 20 ejaculations following vasectomy. Sexual intercourse can typically be resumed within a week following the procedure, but pregnancy is still possible as viable sperm may be present in the ejaculate. Therefore, another method of birth control must be used after vasectomy until semen analysis confirms azoospermia.

(Choices A and B) Sexual desire and satisfaction levels remain the same or even increase (no fear of pregnancy) after vasectomy, and there is no effect on attaining or maintaining an erection.

(Choice C) Semen is composed primarily of fluid secreted from the seminal vesicles and prostate; spermatozoa make up only 2%-5% of semen by volume. Therefore, vasectomy has little effect on the volume of ejaculate.

(Choice D) After vasectomy, Leydig cells continue to produce testosterone at pre-vasectomy levels.

Educational objective:

After vasectomy, viable sperm remain in the portion of the vas deferens distal to the ligation. Patients can

ligation. Patients can still have **viable sperm** in the distal vas for 3 months and at least 20 ejaculations following vasectomy. Sexual intercourse can typically be resumed within a week following the procedure, but pregnancy is still possible as viable sperm may be present in the ejaculate. Therefore, another method of birth control must be used after vasectomy until semen analysis confirms azoospermia.

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Educational objective:
After vasectomy, viable sperm remain in the portion of the vas deferens distal to the ligation. Patients can still have viable sperm in the ejaculate for 3 months and at least 20 ejaculations.

References

- How little is enough? The evidence for post-vasectomy testing.

An infant born to a 22-year-old female has ambiguous genitalia. The gonadal cells contain a Y chromosome and there is no uterus on pelvic examination. The absence of a uterus is due to the effects of which of the following substances in the fetal period?

A. Testosterone (T)

B. Dihydrotestosterone (DHT)

C. Dehydroepiandrosterone (DHEA)

D. Luteinizing hormone (LH)

E. Mullerian inhibitory factor (MIF)

Submit

An infant born to a 22-year-old female has ambiguous genitalia. The gonadal cells contain a Y chromosome and there is no uterus on pelvic examination. The absence of a uterus is due to the effects of which of the following substances in the fetal period?

- A. Testosterone (T) (2%)
- B. Dihydrotestosterone (DHT) (3%)
- C. Dehydroepiandrosterone (DHEA) (1%)
- D. Luteinizing hormone (LH) (0%)
- ✓ E. Mullerian inhibitory factor (MIF) (91%)

Correct

91% Answered correctly

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Explanation

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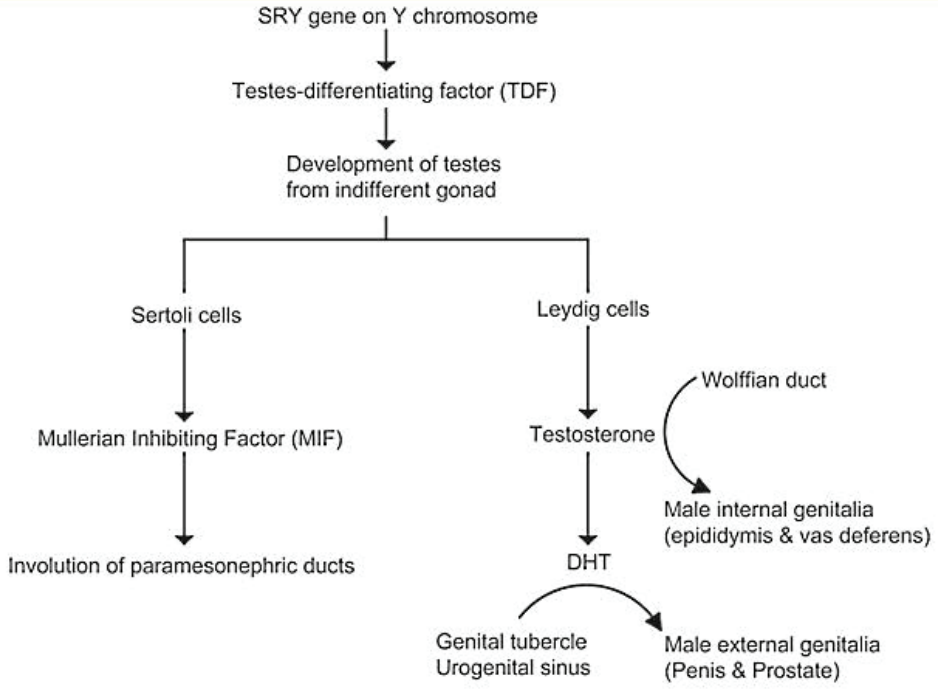

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swellings. Differentiation of the reproductive system occurs in the following sequence: gonadal

Urogenital sinus (Penis & Prostate)

Although the genetic sex is determined at fertilization, the gonads and external genitalia are initially undifferentiated. During the first six weeks of gestation, the embryo has gonads, paramesonephric (müllerian) ducts *and* mesonephric (wolffian) ducts, a genital tubercle (phallus), urethral folds and genital swellings. Differentiation of the reproductive system occurs in the following sequence: gonadal development, genital duct development, and external genitalia development.

1. Gonadal stage: The primordial germ cells originate near the yolk sac and move towards the genital ridge, forming primitive gonads consisting of germ cells, supporting cells and steroidogenic cells. Under the influence of the SRY gene on the Y chromosome, male gonads begin to secrete testosterone (from Leydig cells) and müllerian-inhibiting factor (from Sertoli cells).
2. Ductal stage: In the male embryo, mullerian-inhibiting factor (MIF) causes the paramesonephric (mullerian) ducts to regress, while the mesonephric ducts develop into the epididymis, ductus deferens and seminal vesicles. In the female embryo, testosterone and MIF are not produced. The müllerian (paramesonephric) ducts give rise to the uterine tubes, uterus, cervix, and upper vagina under the influence of maternal estrogen and the mesonephric ducts regress.
3. Genital stage: The genital tubercle gives rise to glans penis in males and the glans clitoris in females. The urogenital folds transform into the ventral aspect of the penis in males and the labia minora in

influence of maternal estrogen and the mesonephric ducts regress.

3. Genital stage: The genital tubercle gives rise to glans penis in males and the glans clitoris in females. The urogenital folds transform into the ventral aspect of the penis in males and the labia minora in females. The genital swellings become the scrotum in males and the labia majora in females. The urogenital sinus gives rise to the bladder, urethra, prostate, and bulbourethral glands in males. In females it develops into the bladder, urethra, lower vagina and Bartholin glands.

(Choice A) Testosterone is produced by Leydig cells of the testes. During embryogenesis it is responsible for development of the internal male genitalia.

(Choice B) Dihydrotestosterone is an active metabolite of testosterone. During embryonic life it mediates formation of the male external genitalia, while in the adult it is responsible for development of male secondary sex characteristics.

(Choice C) Dehydroepiandrosterone (DHEA) is a sex hormone precursor produced by the adrenal gland. It is not known to play a role in sexual differentiation.

(Choice D) Luteinizing hormone (LH) is produced by the anterior pituitary gland. In the male it is trophic to Leydig cells and stimulates testosterone production. In the female it is responsible for maturation of the ovarian follicles, ovulation, and formation of the corpus luteum.

(Choice B) Dihydrotestosterone is an active metabolite of testosterone. During embryonic life it mediates formation of the male external genitalia, while in the adult it is responsible for development of male secondary sex characteristics.

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Educational Objective:
The embryonic testis secretes testosterone and müllerian inhibiting factor (MIF). MIF is responsible for regression of the paramesonephric (müllerian) ducts that normally give rise to the internal genitalia in the female fetus. Testosterone mediates development of male internal genitalia and DHT mediates development of the external genitalia.

Embryology	Male Reproductive System	Infertility
Subject	System	Topic

A 31-year-old man comes to the emergency department complaining of right-sided scrotal pain and swelling that has gradually worsened over the last 3 days. His temperature is 38.3 C (101 F). On physical examination, his right hemiscrotum is warm, tender, and erythematous. The cremasteric reflex is present. A scrotal ultrasound reveals a fluid collection consistent with a superficial scrotal abscess. Which of the following lymph node groups is most likely to be tender and swollen?

A. Common iliac
B. Inferior mesenteric
C. Infraclavicular
D. Para-aortic
E. Superficial inguinal

Submit

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- A. Common iliac (2%)
- B. Inferior mesenteric (1%)
- C. Infraclavicular (0%)
- ✗ D. Para-aortic (23%)
- ✓ E. Superficial inguinal (71%)

Incorrect
Correct answer
E

71%
Answered correctly

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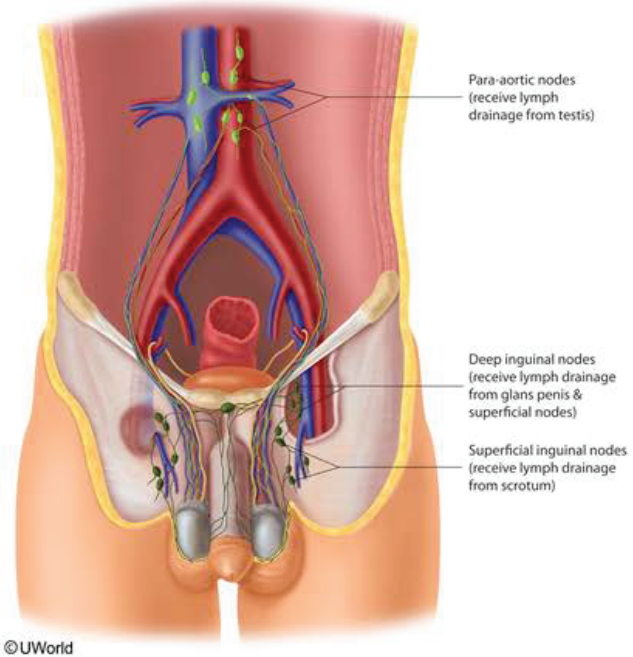
Lymph vessels & nodes of male genitalia



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Lymphatic drainage of the scrotum occurs via the superficial inguinal lymph nodes. These lymph nodes drain nearly all cutaneous lymph from the umbilicus to the feet, including the external genitalia and anus (up to the dentate line). The exceptions are the testis, glans penis, and the cutaneous portion of the posterior calf. Lymph from the testes drains directly into the para-aortic (retroperitoneal) lymph nodes **(Choice D)**. Lymph from the glans penis and the cutaneous portion of the posterior calf drains into the deep inguinal lymph nodes. The superficial inguinal lymph nodes also drain into the deep inguinal lymph nodes.

(Choice A) The common iliac nodes are located alongside the common iliac artery and drain the internal and external iliac nodes. The external iliac nodes receive lymph from the deep inguinal lymph nodes.

(Choice B) The inferior mesenteric nodes drain the structures supplied by branches of the inferior mesenteric artery (eg, the left colic, sigmoid, and superior rectal arteries). Thus, these nodes drain the descending and sigmoid colon as well as the upper part of the rectum, and their efferents drain into the pre-aortic nodes.

(Choice C) Infraclavicular lymph nodes are found beside the cephalic vein between the pectoralis major and deltoid, immediately below the clavicle. They drain lymph from portions of the upper limb and breast.

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(Choice C) Infraclavicular lymph nodes are found beside the cephalic vein between the pectoralis major and deltoid, immediately below the clavicle. They drain lymph from portions of the upper limb and breast.

Educational objective:
Due to its intra-abdominal origin, lymphatic drainage of the testis is to the para-aortic lymph nodes. In contrast, lymph drainage from the scrotum goes into the superficial inguinal lymph nodes.

Anatomy	Male Reproductive System	Lymphatic drainage
Subject	System	Topic

A 70-year-old man comes to the office due to 3 weeks of unrelenting low back pain. He was grocery shopping when he first noticed the pain. The patient reports no trauma or leg weakness but describes having to strain to urinate. He has a history of hypertension and hyperlipidemia and has not seen a doctor in the past 5 years. His wife died a year ago, and he now lives alone. The patient is a retired construction worker and has a history of tobacco and marijuana use. There is tenderness in the lower vertebral area. Imaging study of the spine reveals several osteoblastic lesions in the lumbar vertebrae. Which of the following structures was most likely involved during the spread of this patient's disease?

- A. Azygos veins
- B. Internal iliac lymph nodes
- C. Pampiniform plexus
- D. Paraaortic lymph nodes
- E. Prostatic venous plexus
- F. Vertebral artery

shopping when he first noticed the pain. The patient reports no trauma or leg weakness but describes having to strain to urinate. He has a history of hypertension and hyperlipidemia and has not seen a doctor in the past 5 years. His wife died a year ago, and he now lives alone. The patient is a retired construction worker and has a history of tobacco and marijuana use. There is tenderness in the lower vertebral area. Imaging study of the spine reveals several osteoblastic lesions in the lumbar vertebrae. Which of the following structures was most likely involved during the spread of this patient's disease?

A. Azygos veins (1%)
B. Internal iliac lymph nodes (24%)
C. Pampiniform plexus (4%)
D. Paraaortic lymph nodes (13%)
E. Prostatic venous plexus (53%)
F. Vertebral artery (3%)

Correct

53%
Answered correctly

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This elderly man with new back pain, urinary symptoms, and osteoblastic lesions in the lumbar spine likely has prostate cancer with metastases to the bone. After regional lymph nodes, liver, and lungs, the skeletal system is the fourth most common site of **metastases**, which usually disseminate hematogenously. Cancers of the pelvis, including the prostate, spread to the lumbosacral spine via the **vertebral venous plexus** (VVP). The VVP communicates with a number of venous networks, including the **prostatic venous plexus**, which receives the venous supply from the prostate, penis, and bladder. It runs up the entire spinal column and connects with the venous supply of the brain via a valveless system, which allows for bidirectional flow and regulation of intracranial pressure. This venous connection to the cerebral circulation may help explain the propensity of tumors to metastasize to the brain.

(Choices A and F) The VVP also communicates with the azygos vein in the chest, which explains in part why breast and lung cancers frequently metastasize to the thoracic spine. Similarly, due to pulmonary venous drainage into the left side of the heart, lung tumors often spread systemically via the arterial system.

(Choices B and D) Although lymph nodes are the most common sites of metastasis in general, lymphatic spread to the skeletal system is very rare.

(Choice C) The pampiniform plexus receives venous drainage from the testis, epididymis, and ductus

system.

(Choices B and D) Although lymph nodes are the most common sites of metastasis in general, lymphatic spread to the skeletal system is very rare.

(Choice C) The pampiniform plexus receives venous drainage from the testis, epididymis, and ductus deferens and drains into the testicular veins.

Educational objective:

The skeletal system is a common site of metastasis due to hematogenous seeding. Cancers of the pelvis, including the prostate, spread to the lumbosacral spine via the vertebral venous plexus, which in turn communicates with a number of venous networks, including the prostatic venous plexus.

References

- The cerebrospinal venous system: anatomy, physiology, and clinical implications.
- The craniospinal venous system.
- Physiopathology of spine metastasis.

Anatomy Male Reproductive System Prostate cancer

A 35-year-old man is seen in the office due to heaviness in his lower abdomen. He has a history of bilateral cryptorchidism in childhood and underwent orchiopexy at age 14 months. The patient is otherwise healthy and takes no medications. Physical examination shows enlargement of both testicles. Scrotal ultrasound reveals bilateral testicular masses consistent with testicular germ cell tumor. CT scans of the chest, abdomen, and pelvis do not reveal any lymph node metastasis. The patient undergoes bilateral orchiectomy. Which of the following long-term physiologic changes are most likely to occur as a result of treatment in this patient?

A. Decrease in subcutaneous fat
B. Decreased prostate glandular volume
C. Increase in lean body weight
D. Increase in trabecular bone density
E. Increased prostate stroma volume

Submit

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A. Decrease in subcutaneous fat (1%)
B. Decreased prostate glandular volume (85%)
C. Increase in lean body weight (2%)
D. Increase in trabecular bone density (4%)
E. Increased prostate stroma volume (5%)

Effects of androgen deprivation in men	
Body composition	• Decreased lean body weight • Increased total weight & subcutaneous fat
Skin, hair & breast	• Dry skin • Decreased body hair • Breast enlargement
Skeletal	• Decreased bone density • No change in adult skeletal dimensions
Genitourinary	• Decreased prostate volume
Reproductive/sexual	• Decreased libido • Erectile dysfunction • Decreased sperm count

This patient has undergone **bilateral orchiectomy** for testicular germ cell tumor. Bilateral orchiectomy is also performed for treatment of metastatic prostate cancer and as a component of gender confirming

- Decreased sperm count

This patient has undergone **bilateral orchiectomy** for testicular germ cell tumor. Bilateral orchiectomy is also performed for treatment of metastatic prostate cancer and as a component of gender-confirming surgery in transgender patients. With bilateral testicular loss or failure (eg, mumps orchitis), extragonadal androgen sources (eg, adrenals) are typically inadequate to replace the loss of testosterone, resulting in a **hypogonadal state**.

The prostate is dependent on the trophic effects of dihydrotestosterone (the primary active testosterone metabolite), which is derived from testosterone via 5-alpha-reductase activity in local tissues. Loss of the normal supply of testosterone leads to marked **atrophy of the glandular component of the prostate**. The effects on the prostate stroma are relatively less, but apoptosis may be seen in stromal cells, and the combined effect is a significant **decrease in prostatic volume (Choice E)**. Other genitourinary and sexual effects of hypogonadism include erectile dysfunction, decreased ejaculate volume, and decreased libido.

(Choices A and C) Loss of testosterone leads to significant changes in body composition over time. Testosterone induces increased protein synthesis in myocytes, so hypogonadal patients typically experience a decrease in muscle mass/lean body weight. However, subcutaneous fat increases, and patients frequently experience a small net increase in total body weight.

combined effect is a significant **decrease in prostatic volume (Choice E)**. Other genitourinary and sexual effects of hypogonadism include erectile dysfunction, decreased ejaculate volume, and decreased libido.

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(Choice D) Testosterone induces proliferation and differentiation of osteoblasts. If bilateral orchiectomy is performed after skeletal maturity, bone dimensions do not change, but trabecular bone density decreases (osteoporosis).

Educational objective:
Following bilateral orchiectomy, extragonadal androgen sources are inadequate to replace the loss of testosterone, causing a hypogonadal state. Loss of testosterone leads to changes in body composition, including decreased lean body weight, increased subcutaneous fat, and decreased bone density. Loss of testosterone also leads to a significant decrease in prostate volume.

Physiology Male Reproductive System Male sexual dysfunction

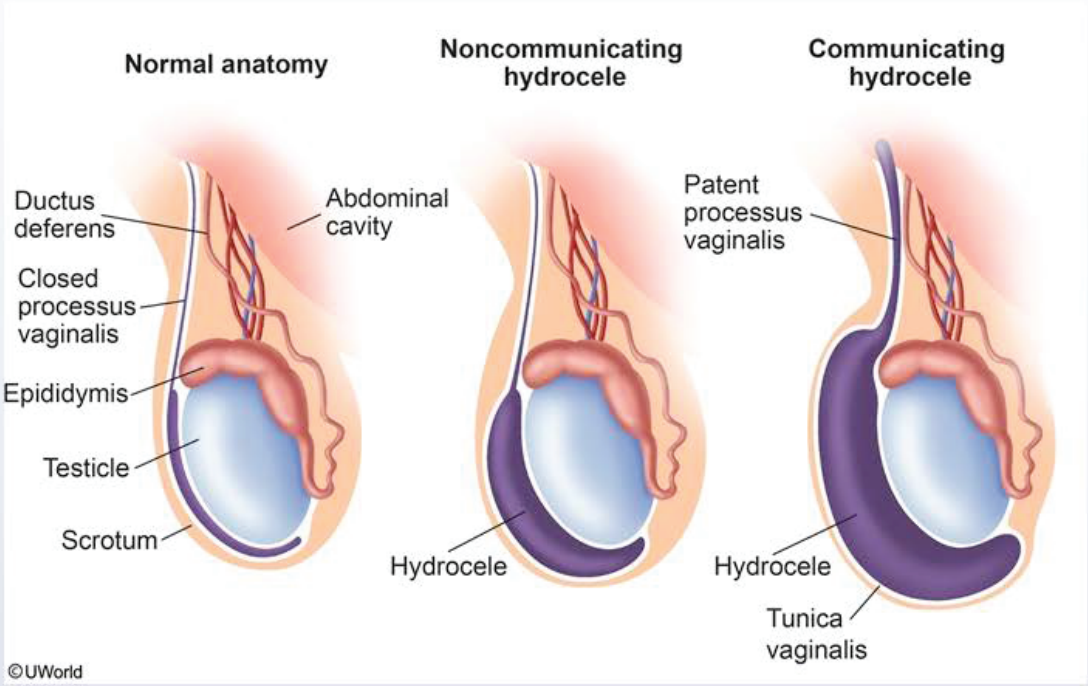
A 2-week-old boy is brought to the office for his first newborn evaluation. The boy has had persistent swelling of his left scrotum, but there has been no noticeable discomfort. Review of birth records indicates that the patient was born at 37 weeks gestation after an uncomplicated vaginal delivery. He has been breastfeeding well with normal voiding and stooling. Physical examination shows bilateral descended testicles with an enlarged, fluctuant left hemi-scrotum that transilluminates brightly. No inguinal or abdominal masses are present. The most likely cause of this patient's condition is a swelling in which of the following locations?

- A. Caput of the epididymis
- B. Cremasteric fascia
- C. External spermatic fascia
- D. Internal spermatic fascia
- E. Pampiniform plexus
- F. Tunica albuginea
- G. Tunica vaginalis

swelling of his left scrotum, but there has been no noticeable discomfort. Review of birth records indicates that the patient was born at 37 weeks gestation after an uncomplicated vaginal delivery. He has been breastfeeding well with normal voiding and stooling. Physical examination shows bilateral descended testicles with an enlarged, fluctuant left hemi-scrotum that transilluminates brightly. No inguinal or abdominal masses are present. The most likely cause of this patient's condition is a swelling in which of the following locations?

A. Caput of the epididymis (1%)
B. Cremasteric fascia (1%)
C. External spermatic fascia (2%)
D. Internal spermatic fascia (2%)
E. Pampiniform plexus (8%)
F. Tunica albuginea (9%)
G. Tunica vaginalis (74%)

Explanation



This patient's clinical presentation is consistent with a congenital, **communicating hydrocele**, a collection

vaginalis

This patient's clinical presentation is consistent with a congenital, **communicating hydrocele**, a collection of **peritoneal fluid** within the **tunica vaginalis**. During embryogenesis, the testis descends through the inguinal canal, drawing with it a diverticulum of peritoneum into the scrotum. This peritoneal tissue is known as the processus vaginalis. Normally, the communication between the processus vaginalis and the peritoneum is obliterated, and the tunica vaginalis is the remaining tissue overlying the testis and epididymis. A communicating hydrocele results when the **processus vaginalis** remains **patent** and allows peritoneal fluid to accumulate in the tunica vaginalis. This type of hydrocele is common in newborns and presents as a painless scrotal swelling that transilluminates.

(Choice A) The epididymis is a coiled tube posterior to the testicle that is responsible for the storage, maturation, and transportation of sperm. The caput, or head, of the epididymis is the superior-most aspect of the tube that stores sperm prior to maturation. Inflammation of the epididymis, or epididymitis, is classically associated with *Gonorrhea* and *Chlamydia* infection.

(Choices B, C, and D) The spermatic cord is a collection of structures that originate in the abdominal cavity and course downward toward the testes. It is covered by 3 layers: internal spermatic fascia, cremasteric fascia, and external spermatic fascia. The internal spermatic fascia immediately overlies the

classically associated with *Gonorrhea* and *Chlamydia* infection.

(Choices B, C, and D) The spermatic cord is a collection of structures that originate in the abdominal cavity and course downward toward the testes. It is covered by 3 layers: internal spermatic fascia, cremasteric fascia, and external spermatic fascia. The internal spermatic fascia immediately overlies the spermatic cord and is derived from the transversalis fascia. The cremasteric fascia arises from the internal oblique abdominal muscle. The external spermatic fascia is derived from the external oblique abdominal muscle. This is the outermost layer of the spermatic cord and lies deep to the dartos muscle and scrotal fascia.

(Choice E) The pampiniform plexus is a collection of veins within the spermatic cord. Distension of these veins leads to a varicocele and is clinically described as a palpable "bag of worms."

(Choice F) The tunica albuginea is the fibrous tissue that immediately overlies the testicles (ie, beneath the tunica vaginalis) and the corpora cavernosa of the penis. In Peyronie disease, excess collagen formation within the tunica albuginea can cause significant pain and curvature of the penis.

Educational objective:

A communicating hydrocele results when serous fluid accumulates within the tunica vaginalis in the setting of a patent processus vaginalis. It presents as a painless swelling that transilluminates on examination.

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Educational objective:

A communicating hydrocele results when serous fluid accumulates within the tunica vaginalis in the setting of a patent processus vaginalis. It presents as a painless swelling that transilluminates on examination.

References

- Evaluation of scrotal masses.
- Hernias and hydroceles.

A 59-year-old man is being evaluated for markedly elevated prostate-specific antigen levels. He has no bone pain or urinary symptoms. The patient has no chronic medical conditions or surgical history. His father died of prostate cancer. Vital signs are normal. Digital rectal examination reveals an indurated prostate with no palpable nodules. The remainder of the examination is normal. Prostate biopsy is planned. Which of the following is the best way to obtain a diagnosis in this patient?

A. Cystoscopy guided; multiple random biopsies of the prostate
B. Cystoscopy guided; single biopsy of the central portion of the prostate
C. Transperineal approach; fine-needle aspiration of the prostate
D. Transrectal route; multiple random biopsies of the prostate
E. Transrectal route; single biopsy from the center of the gland

Submit

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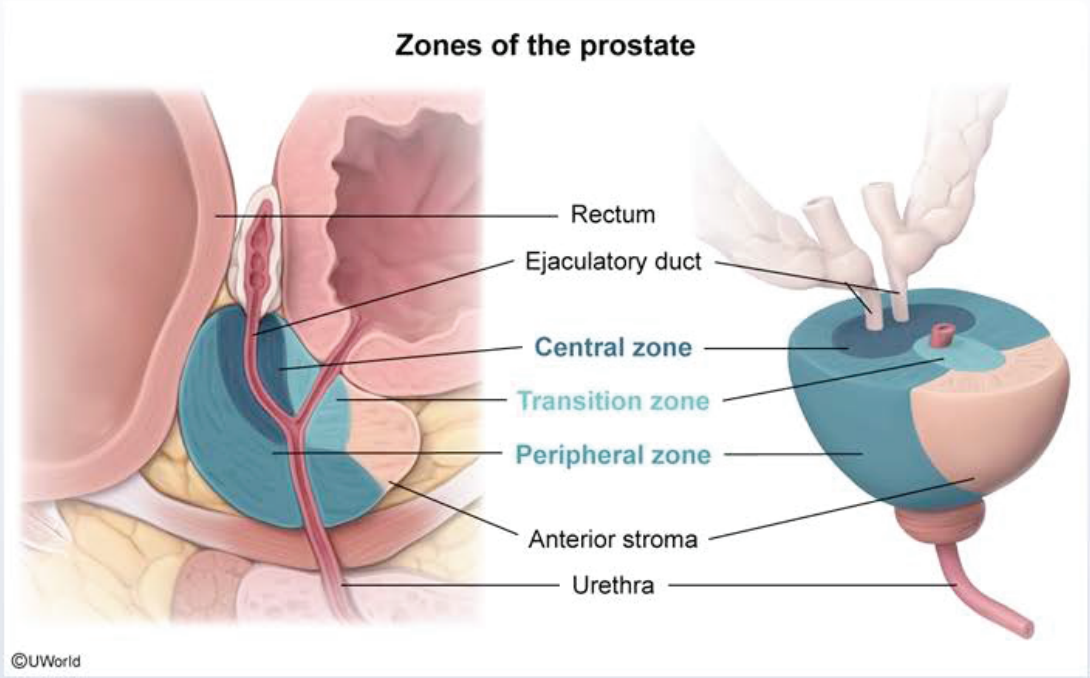
A. Cystoscopy guided; multiple random biopsies of the prostate (19%)
B. Cystoscopy guided; single biopsy of the central portion of the prostate (6%)
C. Transperineal approach; fine-needle aspiration of the prostate (9%)
✓ D. Transrectal route; multiple random biopsies of the prostate (56%)
E. Transrectal route; single biopsy from the center of the gland (8%)

Correct

56% Answered correctly

42 secs Time Spent

12/06/2020 Last Updated



The **prostate** is a walnut-sized gland that encases the urethra and vas deferens. It abuts the urinary bladder superiorly and the rectum posteriorly and is composed of 3 distinct zones:

The **prostate** is a walnut-sized gland that encases the urethra and vas deferens. It abuts the urinary bladder superiorly and the rectum posteriorly and is composed of 3 distinct zones:

- The **peripheral zone** is largely glandular and is the site of **>85%** of prostate **adenocarcinoma**. Because this zone borders the rectum, patients with suspected prostate cancer generally undergo **transrectal ultrasound–guided biopsy**. In this procedure, transrectal ultrasound identifies the borders of the prostate and suspicious hypoechoic lesions; **multiple core biopsies** (usually 10-12) are then obtained from random locations within the apical and far-lateral prostate (peripheral zone). Because the distal urethra passes through only a small portion of the peripheral zone, prostate cancer does not typically present with urinary symptoms (eg, voiding difficulty, hematuria).
- The **central zone** surrounds the ejaculatory duct. This zone is primarily composed of stroma elements; prostate cancer rarely develops in this area.
- The **transition zone** surrounds the **urethra**. This is the primary site of benign prostatic hyperplasia. Because only 10% of prostate cancers arise in this region, cystoscopy approaches (via the urethra) are not typically used to sample the prostate for cancer **(Choices A and B)**.

(Choice C) Fine-needle aspiration is not recommended for the diagnosis of prostate cancer because

- The **transition zone** surrounds the **urethra**. This is the primary site of benign prostatic hyperplasia. Because only 10% of prostate cancers arise in this region, cystoscopy approaches (via the urethra) are not typically used to sample the prostate for cancer **(Choices A and B)**.

(Choice C) Fine-needle aspiration is not recommended for the diagnosis of prostate cancer because tissue architecture is lost during sampling. Transperineal core biopsies are occasionally used to diagnose prostate cancer in men who cannot tolerate the transrectal approach.

(Choice E) The diagnosis of prostate cancer requires multiple core biopsies to obtain adequate sampling of the prostate. A single biopsy would dramatically increase the risk of a false negative result. Furthermore, the central portion of the gland is less likely to develop prostate cancer than the peripheral portion.

Educational objective:
Most prostate cancer arises in the peripheral zone of the gland, which abuts the rectum. Therefore, prostate biopsies are primarily obtained via the transrectal approach; multiple random core samples of the prostate are typically taken. Because only a small part of the peripheral zone encases the distal urethra, patients with prostate cancer do not typically present with urinary symptoms.

A 66-year-old man comes to the office for follow-up of metastatic prostate cancer. He was diagnosed 12 months ago, when he was found to have a single bony metastasis. The patient declined orchiectomy and was treated with a long-acting gonadotropin-releasing hormone agonist. While on this therapy, he developed nocturnal pain in the area of the bony metastasis and was found to have a rising level of prostate-specific antigen. Flutamide was then added to his initial therapy and led to significant pain relief and a decrease in the size of the primary tumor. Which of the following mechanisms is the best explanation for the effects of flutamide in this patient?

A. Decreased androgen aromatization
B. Decreased Leydig cell stimulation
C. Decreased peripheral androgen conversion
D. Impaired androgen-receptor interaction
E. Inhibition of androgen synthesis

Submit

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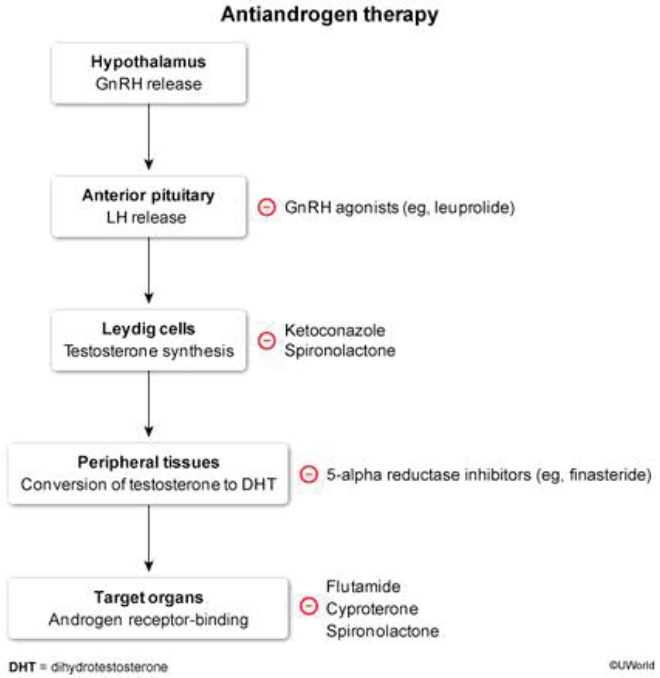
A. ~~Decreased androgen aromatization~~ (7%)
B. ~~Decreased Leydig cell stimulation~~ (5%)
C. ~~Decreased peripheral androgen conversion~~ (21%)
D. Impaired androgen-receptor interaction (56%)
E. Inhibition of androgen synthesis (9%)

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

Prostate cancer is **testosterone-dependent** and can be treated in most cases with surgical and/or pharmacologic androgen deprivation. Initial options include bilateral orchiectomy or a gonadotropin-releasing hormone (GnRH) agonist. **Pulsatile** release of GnRH from the hypothalamus stimulates secretion of LH from the anterior pituitary and leads to increased testosterone production. However, **constant** GnRH activity causes down-regulation of the GnRH receptors on pituitary gonadotrophin cells, which suppresses LH secretion. Therefore, long-acting GnRH agonists (eg, leuprolide) paradoxically cause a decrease in testicular Leydig cell stimulation **(Choice B)**. The use of long-acting GnRH agonists can be associated with a **transient** rise in LH and testosterone levels following treatment initiation. As a result, antiandrogens are sometimes prescribed concurrently to limit the tumor-stimulating effects of this initial testosterone rise.

Flutamide is a nonsteroid agent that acts as a **competitive testosterone receptor inhibitor**. Prevention of androgen-receptor binding blocks the stimulatory effect of androgens on the primary tumor and metastases and leads to a reduction in their size (improving symptoms such as bone pain and urinary obstruction).

(Choice A) Aromatase inhibitors (eg, anastrozole) decrease the peripheral conversion of androgens to estrogen and are used in postmenopausal women with estrogen receptor-positive breast cancer. They do

(Choice A) Aromatase inhibitors (eg, anastrozole) decrease the peripheral conversion of androgens to estrogen and are used in postmenopausal women with estrogen receptor-positive breast cancer. They do not lower androgen levels and are not used in the treatment of prostate cancer.

(Choice C) Finasteride decreases peripheral conversion of testosterone to dihydrotestosterone by inhibiting 5-α-reductase. It is used for treatment of benign prostatic hyperplasia and male-pattern baldness.

(Choice E) Ketoconazole is a weak antiandrogen that decreases synthesis of steroid hormones in the gonads and adrenals. Flutamide does not inhibit testosterone production by Leydig cells.

Educational objective:
Flutamide is a nonsteroid anti-androgen that acts as a competitive inhibitor of testosterone receptors. It is used in combination with long-acting gonadotropin-releasing hormone agonists for the treatment of prostate cancer.

References

- Non-steroidal antiandrogen monotherapy compared with luteinizing hormone-releasing hormone agonists or surgical castration monotherapy for advanced prostate cancer: a Cochrane systematic review.

A 60-year-old man comes to the office to discuss sexual symptoms. Eight weeks ago, the patient was admitted to the hospital with a non–ST-elevation myocardial infarction, and a drug-eluting stent was successfully placed in the culprit coronary artery. The patient now has no cardiovascular symptoms, including when climbing stairs or taking long walks. Since discharge, he has had difficulty maintaining an erection and delayed ejaculation during sexual intercourse, but he has normal libido and regular nocturnal erections. Medications include metoprolol, rosuvastatin, aspirin, and ticagrelor. Vital signs and physical examination are normal. Which of the following is the most likely cause of this patient's sexual dysfunction?

A. Aortoiliac occlusion
B. Bladder neck obstruction
C. Metoprolol adverse effect
D. Psychogenic sexual dysfunction
E. Testosterone deficiency

admitted to the hospital with a non–ST-elevation myocardial infarction, and a drug-eluting stent was successfully placed in the culprit coronary artery. The patient now has no cardiovascular symptoms, including when climbing stairs or taking long walks. Since discharge, he has had difficulty maintaining an erection and delayed ejaculation during sexual intercourse, but he has normal libido and regular nocturnal erections. Medications include metoprolol, rosuvastatin, aspirin, and ticagrelor. Vital signs and physical examination are normal. Which of the following is the most likely cause of this patient's sexual dysfunction?

- A. Aortoiliac occlusion (2%)
- B. Bladder neck obstruction (0%)
- C. Metoprolol adverse effect (48%)
- ✓ D. Psychogenic sexual dysfunction (47%)
- E. Testosterone deficiency (0%)

Correct

47%

01 min, 29 secs

11/11/2020

Explanation

Sexual performance anxiety/psychogenic ED	
Causes & risk factors	• Marital/relational stress, conflict • Major psychosocial trauma (loss of job or loved one) • Severe medical illness (stroke, myocardial infarction) • Mood, anxiety disorders
Features	• Abrupt onset, clear precipitating event or stressor • Situational ED (normal nocturnal/nonsexual erections) • Impaired or premature orgasm
Management	• Cognitive-behavioral therapy • Couples/relational therapy

ED = erectile dysfunction.

Erectile dysfunction (ED) is characterized by an inability to initiate or maintain an erection adequate for

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Erectile dysfunction (ED) is characterized by an inability to initiate or maintain an erection adequate for sexual intercourse. Causes can be categorized as organic (eg, hypogonadism, arterial insufficiency, neurologic impairment) or psychogenic.

Psychogenic ED is common in patients with preexisting mood or anxiety disorders but can also occur abruptly following a stressful precipitating event:

- Prolonged illness: Patients may be hesitant or unsure how to initiate sexual activity.
- Severe, acute illness: Patients may believe the illness can be caused or worsened by sexual activity. This is especially common in those with cardiovascular disease (eg, stroke, myocardial infarction), who are often concerned that sexual activity may strain the heart and lead to further cardiac events.
- Surgical procedures: Patients may be embarrassed by their appearance (eg, surgical scar) or body odor (eg, incontinence, colostomy).
- Loss of loved one: Patients may experience survivor guilt or feel fearful about the future.

Psychogenic ED is often **situational**, with normal erections at night or during masturbation but impaired erections when with a partner. This patient has situational ED despite normal libido following an acute,

- Loss of loved one. Patients may experience survivor guilt or feel fearful about the future.

Psychogenic ED is often **situational**, with normal erections at night or during masturbation but impaired erections when with a partner. This patient has situational ED despite normal libido following an acute, severe illness, suggesting **psychogenic sexual dysfunction** (ie, performance anxiety) rather than an organic etiology.

(Choice A) Organic ED is common in patients with cardiovascular disease due to systemic arterial insufficiency and comorbid conditions (eg, diabetes) that impair erectile function. However, onset typically occurs gradually, rather than abruptly following a stressful event, and nocturnal erections are impaired as well. In addition, aortoiliac occlusion is often associated with pain in the buttocks, posterior thigh, or calf during exercise; this patient has normal exercise tolerance.

(Choice B) Bladder neck obstruction (eg, benign prostatic hyperplasia [BPH]) can reduce semen volume. Laxity of the musculature at the bladder outlet, which can occur following surgical repair of BPH, can lead to retrograde ejaculation of semen into the bladder. However, erections are typically normal unless the patient is taking a 5-alpha reductase inhibitor (eg, finasteride).

(Choice C) Some cardiovascular medications, such as beta blockers (eg, metoprolol) and thiazide diuretics, can cause ED, but nocturnal/nonsexual erections are also affected.

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(Choice C) Some cardiovascular medications, such as beta blockers (eg, metoprolol) and thiazide diuretics, can cause ED, but nocturnal/nonsexual erections are also affected.

(Choice E) Testosterone deficiency causes ED with decreased libido and loss of nocturnal erections. This patient's normal libido suggests adequate testosterone levels.

Educational objective:
Psychogenic erectile dysfunction often begins abruptly following severe medical (eg, myocardial infarction) or emotional stressors. The symptoms are often situational, with normal erections at night or during masturbation but impaired with a partner. Libido is often normal.

References

- Sexual performance anxiety.

A 54-year-old man comes to the office due to difficulty maintaining an erection for the last several weeks. He says, "One night I was having sex with my wife and could not maintain an erection. Since then, it has continued to be a problem." The patient still has morning erections. His medical history is significant for hypertension, coronary artery disease, and depression. He has been married for 20 years but reports that he and his wife have been arguing since he began spending more time at work following a promotion 2 months ago. His current medications include amlodipine, lisinopril, and bupropion. Physical examination is unremarkable. Which of the following is the most likely cause of this patient's erectile dysfunction?

A. Advancing age
B. Antidepressant-induced sexual dysfunction
C. Antihypertensive-induced adverse effect
D. Psychological distress
E. Vascular insufficiency

Submit

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A. Advancing age (1%)
B. Antidepressant-induced sexual dysfunction (5%)
C. Antihypertensive-induced adverse effect (3%)
✓ D. Psychological distress (86%)
E. Vascular insufficiency (2%)

86% 56 secs 09/07/2020

The temporal association between this patient's arguments with his wife and subsequent onset of **erectile dysfunction** (ED) makes **psychogenic** factors the most likely cause of his ED. The presence of **spontaneous nocturnal erections** is another important diagnostic clue as this demonstrates the integrity of neurologic reflexes and corpus cavernosa blood flow. Loss of normal nocturnal erections occurs in men with organic ED but is not seen with psychogenic etiologies.

ED can be caused by organic factors, psychogenic factors, or a combination of both. Psychogenic causes include performance anxiety, depression, sexual trauma, and/or relationship problems and are typically associated with an **abrupt onset** triggered by stress, as in this patient. In contrast, men suffering from organic causes of ED (eg, vascular insufficiency) tend to have a slower progression of symptoms, with intermittent ED later becoming more persistent in nature **(Choice E)**.

(Choice A) There tends to be an increase in the incidence of ED with advancing age. However, the sudden onset of this patient's dysfunction during a time of relationship and work stress makes a psychogenic cause more likely.

(Choices B and C) Antidepressants, particularly selective serotonin reuptake inhibitors, have been associated with sexual dysfunction. However, the norepinephrine-dopamine reuptake inhibitor bupropion

sudden onset of this patient's dysfunction during a time of relationship and work stress makes a psychogenic cause more likely.

(Choices B and C) Antidepressants, particularly selective serotonin reuptake inhibitors, have been associated with sexual dysfunction. However, the norepinephrine-dopamine reuptake inhibitor bupropion has not been associated with sexual dysfunction. Of the antihypertensive agents, thiazide diuretics and sympathetic blockers (eg, clonidine, methyldopa) have the greatest risk for ED. Angiotension-converting enzyme inhibitors (eg, lisinopril) and calcium channel blockers (eg, amlodipine) have the least risk.

Educational objective:

Psychogenic causes of erectile dysfunction include performance anxiety, depression, sexual trauma, relationship problems, and stress. Important clues include sudden-onset and normal nocturnal erections.

References

- The 2018 revision to the process of care model for evaluation of erectile dysfunction.

Pathology	Male Reproductive System	Male sexual dysfunction
Subject	System	Topic

A 66-year-old man comes to the emergency department due to a 3-day history of fever, chills, dysuria, and perineal pain. The patient has never had similar symptoms before, although he has had occasional nocturia and urinary hesitancy over the last 2 years. His other medical conditions include type 2 diabetes mellitus and hypertension. The patient does not use tobacco, alcohol, or illicit drugs. He has not traveled recently and is not sexually active. Temperature is 39 C (102.2 F), blood pressure is 124/78 mm Hg, and pulse is 106/min. The abdomen is soft and nontender with no costovertebral angle tenderness. Digital rectal examination shows a smoothly enlarged and tender prostate. External genitalia are normal with no scrotal tenderness. There is no urethral discharge. The remainder of the examination shows no abnormalities. Urinalysis reveals bacteriuria and pyuria. Which of the following pathogens is most likely responsible for this patient's current symptoms?

- A. *Chlamydia trachomatis*
- B. *Coccidioides immitis*
- C. *Escherichia coli*
- D. *Mycoplasma hominis*
- E. *Neisseria gonorrhoeae*

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- B. *Coccidioides immitis*
- C. *Escherichia coli*
- D. *Mycoplasma hominis*
- E. *Neisseria gonorrhoeae*
- F. *Staphylococcus aureus*
- G. *Staphylococcus saprophyticus*
- H. *Ureaplasma urealyticum*

Submit

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- A. *Chlamydia trachomatis* (1%)
- B. *Coccidioides immitis* (0%)
- ✓ C. *Escherichia coli* (91%)
- D. *Mycoplasma hominis* (0%)
- E. *Neisseria gonorrhoeae* (0%)
- F. *Staphylococcus aureus* (2%)
- G. *Staphylococcus saprophyticus* (0%)
- H. *Ureaplasma urealyticum* (2%)

Acute bacterial prostatitis	
Etiology	• Reflux of urine & organisms from bladder & urethra • Mostly **gram-negative bacilli** (majority *Escherichia coli*)
Clinical presentation	• Systemic symptoms (eg, fever, chills) • Lower urinary tract symptoms (eg, dysuria, urine retention, pelvic pain) • Examination: swollen, tender prostate
Diagnosis	• Urine Gram stain & culture

This patient has fever, dysuria, and prostatic tenderness, consistent with **acute bacterial prostatitis** (ABP). ABP is most commonly caused by reflux of urine and organisms from the bladder and urethra into the prostatic ducts, although it can occasionally be caused by direct inoculation (eg, prostate biopsy) or hematogenous seeding from remote infection (eg, endocarditis). The risk of developing ABP is greater in patients with diabetes mellitus, anatomic abnormalities (eg, strictures), or bladder catheterization.

Diagnosis	• Urine Gram stain & culture

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As with other urinary tract infections, the most common organisms in ABP include **enteric gram-negative bacilli**, predominantly ***Escherichia coli***, because of virulence factors (eg, adhesins on bacterial fimbriae) that allow it to adhere onto mucosal or urothelial cells. The other bacteria (also gram-negative bacilli) that commonly cause ABP include *Proteus*, *Klebsiella*, *Pseudomonas*.

(Choices A and E) Sexually transmitted organisms (eg, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*) commonly cause urethritis and/or urogenital infections that can involve the prostate, but this typically occurs in younger, sexually active men (this patient is older and not sexually active).

(Choice B) *Coccidioides* infections most commonly cause community-acquired pneumonia in endemic areas (eg, California, Arizona), but they can also cause dermatologic (eg, erythema nodosum or multiforme) or rheumatologic (eg, arthralgias) manifestations.

(Choice B) *Coccidioides* infections most commonly cause community-acquired pneumonia in endemic areas (eg, California, Arizona), but they can also cause dermatologic (eg, erythema nodosum or multiforme) or rheumatologic (eg, arthralgias) manifestations.

(Choices D and H) *Mycoplasma hominis* and *Ureaplasma urealyticum* commonly colonize the genitourinary tract, but they have not been proven to be a significant cause of symptomatic genitourinary infections.

(Choice F) Gram-positive skin flora (eg, *Staphylococcus aureus*) most commonly cause skin and soft tissue infections. Although patients with *S aureus* bacteremia can develop localized infections throughout the body (eg, endocarditis, osteomyelitis, organ abscess), isolated ABP would be rare.

(Choice G) Coagulase-negative staphylococci (eg, *S saprophyticus*) are a common cause of acute cystitis in young women.

Educational objective:
Acute bacterial prostatitis is usually caused by reflux of urine and organisms from the bladder and urethra. The risk is greater in patients with anatomic abnormalities (eg, strictures) or bladder catheterization. *Escherichia coli* is the most common cause of acute bacterial prostatitis and other urinary tract infections because of adhesins on its fimbriae that promote adherence to urothelial or mucosal cells.

A 64-year-old man comes to the office due to urinary frequency, hesitancy, and dribbling. His symptoms began insidiously 5 years ago and have progressively worsened. He has to get up 2 or 3 times each night to urinate. Vital signs are normal. Examination shows a smooth, symmetrically enlarged prostate without nodules or tenderness. There is no suprapubic tenderness. Prostate-specific antigen level is 3.5 ng/mL, creatinine is 1.2 mg/dL, and urinalysis is normal. The patient is started on a new medication. After 6 months of therapy, his urinary symptoms improve and prostate volume decreases by 20%. Which of the following medications is most likely responsible for the decreased prostate volume in this patient?

A. Finasteride
B. Phenazopyridine
C. Tadalafil
D. Tamsulosin
E. Tolterodine

Submit

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- A. Finasteride (82%)
- B. Phenazopyridine (0%)
- C. Tadalafil (1%)
- D. Tamsulosin (14%)
- E. Tolterodine (0%)

Medical therapy for benign prostatic hyperplasia	
Alpha-adrenergic antagonists (eg, terazosin, tamsulosin)	• Relax smooth muscle in bladder neck, prostate capsule & prostatic urethra • Usual first-line therapy • **Adverse effects:** orthostatic hypotension, dizziness
5-alpha-reductase inhibitors (eg, finasteride, dutasteride)	• Inhibit conversion of testosterone to dihydrotestosterone • Reduce prostate gland size • Effectiveness may take 6-12 months • **Adverse effects:** decreased libido, erectile dysfunction
Antimuscarinics (eg, tolterodine)	• Used to treat overactive bladder (urinary frequency, urgency & incontinence) • **Adverse effects:** urine retention, dry mouth

This patient has **benign prostatic hyperplasia** (BPH). BPH is due to the effects of dihydrotestosterone on prostatic epithelial cells and is characterized by progressive prostatic enlargement with age, leading to

This patient has **benign prostatic hyperplasia** (BPH). BPH is due to the effects of dihydrotestosterone on prostatic epithelial cells and is characterized by progressive prostatic enlargement with age, leading to **bladder outlet obstruction** and incomplete bladder emptying. Typical symptoms include urinary frequency, nocturia, hesitancy, and weak urinary stream. The bladder outlet obstruction is made up of a **dynamic component** (smooth muscle tone in the bladder neck, prostate capsule, and prostatic urethra) and a **fixed component** (structural effects of the enlarged prostate).

Alpha adrenergic antagonists (eg, terazosin, tamsulosin) are smooth muscle relaxants that work on the dynamic component of bladder outlet obstruction. They work within days to weeks. However, these drugs do not significantly affect prostate volume **(Choice D)**. **5-alpha reductase inhibitors** (eg, finasteride, dutasteride) inhibit the conversion of testosterone to dihydrotestosterone and address the fixed component of bladder outlet obstruction. Over time, they reduce prostate volume but can take up to 6-12 months to achieve maximal effect.

(Choice B) Phenazopyridine is a urinary analgesic that provides symptomatic relief of dysuria in urinary tract infections. It is not effective for BPH and does not affect prostate volume.

(Choice C) Tadalafil is a phosphodiesterase-5 inhibitor that is primarily used to treat erectile dysfunction. Although some studies have shown symptom improvement in BPH, tadalafil does not significantly decrease

achieve maximal effect.

(Choice B) Phenazopyridine is a urinary analgesic that provides symptomatic relief of dysuria in urinary tract infections. It is not effective for BPH and does not affect prostate volume.

(Choice C) Tadalafil is a phosphodiesterase-5 inhibitor that is primarily used to treat erectile dysfunction. Although some studies have shown symptom improvement in BPH, tadalafil does not significantly decrease prostate volume.

(Choice E) Antimuscarinics (eg, tolterodine) are used to treat overactive bladder symptoms (eg, urinary frequency, urgency, incontinence). They can cause urine retention and are normally used in BPH only once another drug has addressed the bladder outlet obstruction. They do not affect prostate volume.

Educational objective:
5-alpha reductase inhibitors (eg, finasteride, dutasteride) block the conversion of testosterone to dihydrotestosterone in the prostate. These drugs reduce prostate volume in patients with benign prostatic hyperplasia and relieve the fixed component of bladder outlet obstruction.

References

- Finasteride for benign prostatic hyperplasia.

A 22-year-old man comes to the office due to erectile dysfunction and lack of sexual desire. Medical history is unremarkable. The patient is in a stable relationship with his fiancé and does not use tobacco, alcohol, or illicit drugs. Height is 188 cm (6 ft 2 in) and weight is 88 kg (194 lb). Examination shows bilateral gynecomastia, sparse facial hair, and small, firm testes. The penis is normal in size and peripheral vision is normal on confrontation. This patient would most benefit from which of the following?

A. Aromatase inhibitor
B. Gonadotropin
C. Phosphodiesterase 5 inhibitor
D. Selective estrogen receptor modulator
E. Testosterone

Submit

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A. Aromatase inhibitor (32%)
B. Gonadotropin (8%)
C. Phosphodiesterase 5 inhibitor (3%)
D. Selective estrogen receptor modulator (3%)
E. Testosterone (52%)

Incorrect
Correct answer
E

52%
Answered correctly

01 min, 45 secs
Time Spent

11/04/2020
Last Updated

Male primary hypogonadism	
Causes	• Congenital: chromosomal disorders (eg, Klinefelter syndrome), cryptorchidism • Acquired: cancer chemotherapy, hemochromatosis, aging
Clinical findings	• Symptoms: low libido, erectile dysfunction, loss of muscle mass, infertility • Signs: gynecomastia, decreased body hair, low bone density • Laboratory diagnosis: low serum testosterone, high LH & FSH
Treatment	• Transdermal or injected testosterone

This patient has features of testosterone deficiency (ie, **hypogonadism**), including erectile dysfunction, low libido, and gynecomastia. His **tall stature** and **small, firm testes** are consistent with Klinefelter syndrome (KS), which causes hypogonadism due to hyalinization and fibrosis of the testes. Patients who develop hypogonadism prior to puberty, including patients with KS, often have a eunuchoid habitus, sparse body hair, and high-pitched voice, whereas these features are much less pronounced in those who develop hypogonadism later in life.

Primary hypogonadism can be confirmed with **low serum testosterone** associated with **elevated LH**.

Primary hypogonadism can be confirmed with **low serum testosterone** associated with **elevated LH**. Management of male hypogonadism includes **testosterone therapy**, which can improve libido and erectile function, increase bone density, and facilitate muscle development.

(Choice A) Aromatase inhibitors decrease the conversion of androgens to the corresponding estrogens (eg, testosterone to estradiol). Although some experts use aromatase inhibitors as supplemental therapy in KS, the primary defect is inadequate testosterone production, so testosterone therapy should be initiated first.

(Choice B) hCG has bioactivity analogous to that of LH and can be used to stimulate testosterone production in patients with secondary/central hypogonadism (ie, low endogenous LH). However, patients with KS have primary hypogonadism, so gonadotropin therapy is not useful.

(Choice C) Phosphodiesterase 5 inhibitors (eg, sildenafil) can assist in the treatment of erectile dysfunction but would not improve this patient's hormone levels or libido.

(Choice D) Selective estrogen receptor modulators (eg, tamoxifen) are sometimes used to minimize breast enlargement in adolescents with KS. However, nonsurgical interventions are not useful in adults with established gynecomastia.

Educational objective:

first.

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Educational objective:
Management of male hypogonadism includes testosterone therapy, which can improve libido and erectile function, increase bone density, and facilitate muscle development.

References

- Klinefelter syndrome and medical treatment: hypogonadism and beyond.

Pharmacology Male Reproductive System Male sexual dysfunction

A 65-year-old man with benign prostatic hyperplasia has moderately severe symptoms and is started on finasteride. After six months of treatment with finasteride, his symptoms improve markedly and his prostate has regressed in size. Which of the following histological patterns was most likely present at the time of initiation of treatment?

A. Hyperplasia of prostate with predominance of epithelial components
B. Hyperplasia of prostate with predominance of muscular element
C. Hyperplasia of prostate with predominance of collagen
D. Hyperplasia of prostate with predominance of both collagen and smooth muscles

Submit

A 65-year-old man with benign prostatic hyperplasia has moderately severe symptoms and is started on finasteride. After six months of treatment with finasteride, his symptoms improve markedly and his prostate has regressed in size. Which of the following histological patterns was most likely present at the time of initiation of treatment?

- A. Hyperplasia of prostate with predominance of epithelial components (38%)
- B. Hyperplasia of prostate with predominance of muscular element (28%)
- C. Hyperplasia of prostate with predominance of collagen (4%)
- D. Hyperplasia of prostate with predominance of both collagen and smooth muscles (28%)

Incorrect
Correct answer
A

38%
Answered correctly

31 secs
Time Spent

09/21/2020
Last Updated

Explanation

Finasteride is a **5-alpha reductase inhibitor** and it inhibits the conversion of testosterone to dihydrotestosterone. It acts on the **epithelial** components of the prostate gland and produces improvement of symptoms as well as reduction in the size of the gland. There are various histological patterns of BPH. Some patients have predominant epithelial hyperplasia and others have predominant stromal hyperplasia. Those with stromal hyperplasia may have collagen or smooth muscle predominance. Patients with epithelial predominance best respond to treatment with finasteride.

(Choice B, C & D) Alpha-1 blockers produce symptomatic improvement in patients with BPH by their action on smooth muscles present in prostate and bladder base. Patients with smooth muscle predominance best respond to treatment with alpha-1 blockers. Patients with collagen predominance respond neither to finasteride nor to alpha-1 blockers.

Educational objective:
Finasteride acts on epithelium and alpha-1 blockers act on smooth muscles of prostate and bladder base.

Pharmacology	Male Reproductive System	Benign prostatic hyperplasia
Subject	System	Topic

A 5-month-old boy is brought to the office for right-sided scrotal enlargement. The enlargement has been present since birth and increases when he cries or strains to pass a bowel movement. There is no history of trauma or infection. The boy's parents do not believe he is in pain and have not noted discoloration of the area. On ultrasonography, the enlargement is found to be a fluid collection around the right testis. The specific embryologic defect giving rise to this patient's condition can also lead directly to which of the following?

- A. Direct inguinal hernia
- B. Femoral hernia
- C. Hypospadias
- D. Indirect inguinal hernia
- E. Orchitis
- F. Testicular torsion

Submit

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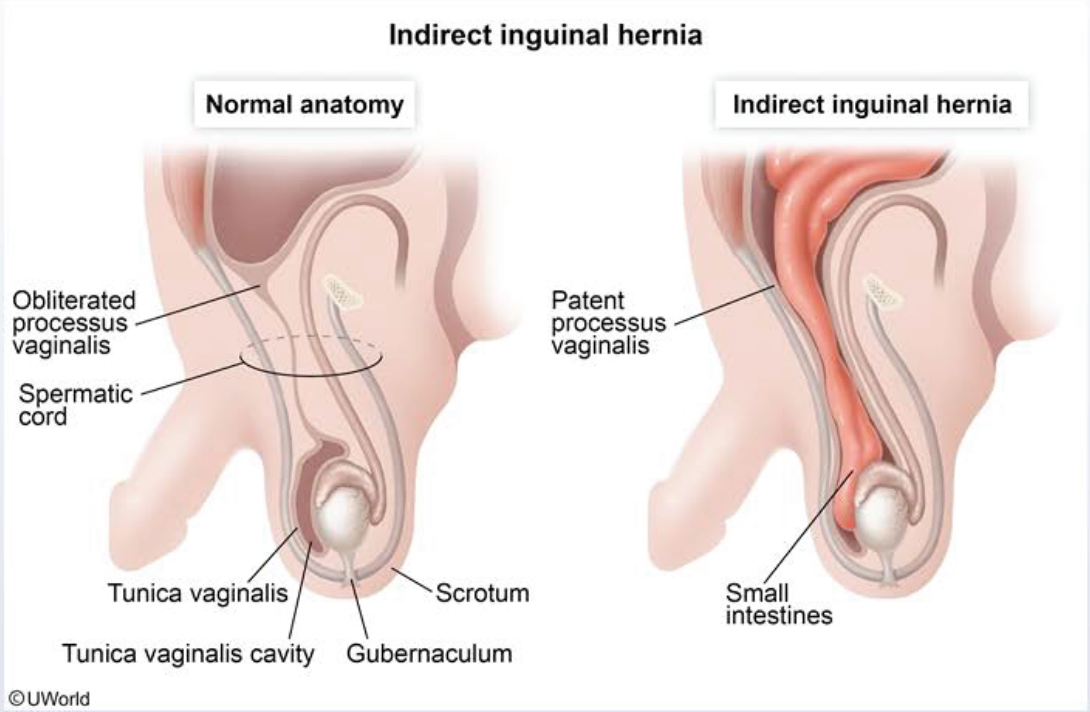
- A. Direct inguinal hernia (14%)
- B. Femoral hernia (0%)
- C. Hypospadias (3%)
- ✓ D. Indirect inguinal hernia (67%)
- E. Orchitis (4%)
- F. Testicular torsion (9%)



Early in normal gestation, the testes are located in the retroperitoneal region and subsequently descend

Tunica vaginalis cavity Gubernaculum

Early in normal gestation, the testes are located in the retroperitoneal region and subsequently descend into the scrotum before birth. During descent, they are accompanied by an evagination of the peritoneum called the processus vaginalis, which then obliterates after descent is complete.

Failure of obliteration of the **processus vaginalis** leads to a persistent connection between the scrotum and the peritoneal cavity through the inguinal canal. If the opening is small and allows for **fluid leakage** only, a communicating hydrocele develops. Diagnosis is made clinically through transillumination of the scrotum; a scrotal ultrasound would reveal fluid surrounding the affected testicle.

If the communication between the peritoneal cavity and the scrotum is large enough to allow for the **passage of abdominal organs**, an **indirect inguinal hernia** develops. Indirect inguinal hernias are common in children. They pass through the deep inguinal ring, are covered by internal spermatic fascia, and are located lateral to the inferior epigastric blood vessels. Hydroceles and indirect inguinal hernias both can present as an asymptomatic scrotal mass that increases in size during Valsalva maneuvers.

(Choice A) Direct inguinal hernias are an acquired protrusion of abdominal contents through a weakness of the abdominal wall (Hesselbach triangle). Direct inguinal hernias do not pass through the inguinal canal and are located medial to the inferior epigastric blood vessels.

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(Choice A) Direct inguinal hernias are an acquired protrusion of abdominal contents through a weakness of the abdominal wall (Hesselbach triangle). Direct inguinal hernias do not pass through the inguinal canal and are located medial to the inferior epigastric blood vessels.

(Choice B) Femoral hernias are an acquired protrusion of abdominal contents through a weakness of the femoral canal. They are the least common type of hernia.

(Choice C) Hypospadias occurs due to incomplete fusion of the urethral folds and presents as a ventrally located urethra.

(Choice E) Orchitis is a non-specific inflammation of the testes that is classically associated with mumps. In young adults and adolescents, it is commonly caused by *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. In older patients, *Escherichia coli* is the most common causative agent.

(Choice F) Testicular torsion is a rotation of the testes around the spermatic cord leading to acute testicular pain. Trauma or a congenitally-horizontal positioning of the testes ("bell clapper deformity") facilitates torsion.

Educational objective:

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Educational objective:
Communicating hydroceles and indirect inguinal hernias are caused by an incomplete obliteration of the processus vaginalis. The resultant connection between the scrotum and abdominal cavity can allow for fluid leakage (hydrocele) or the passage of abdominal contents (indirect inguinal hernia).

References

- Hernias and hydroceles.

A 66-year-old man comes to the office for hypertension follow-up. The patient takes lisinopril and amlodipine, but his blood pressure recordings have been 140-150/85-95 mm Hg over the past 2 office visits. He has had no chest pain or shortness of breath. The patient also reports worsening urinary symptoms over the past year that include hesitancy, straining during urination, poor urinary flow, and waking up once or twice a night to urinate. He feels the symptoms are bothersome but are not affecting his quality of life. The patient has no other medical conditions and does not use tobacco, alcohol, or illicit drugs. Blood pressure is 142/88 mm Hg and pulse is 70/min. Physical examination shows a mildly enlarged, smooth prostate but is otherwise unremarkable. Serum chemistry studies and urinalysis are normal. Which of the following medications would be most effective for treating both of this patient's medical issues?

A. Doxazosin
B. Finasteride
C. Hydralazine
D. Hydrochlorothiazide
E. Metoprolol

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- A. Doxazosin
- B. Finasteride
- C. Hydralazine
- D. Hydrochlorothiazide
- E. Metoprolol
- F. Tamsulosin

Submit

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- A. Doxazosin (39%) ✓
- B. Finasteride (10%)
- C. Hydralazine (1%)
- D. Hydrochlorothiazide (1%)
- E. Metoprolol (1%)
- F. Tamsulosin (44%) ✗

Incorrect
Correct answer

39%
Answered correctly

52 secs
Time Spent

11/30/2020
Last Updated

This patient's obstructive urinary symptoms and mildly enlarged prostate are consistent with **benign prostatic hyperplasia** (BPH). In addition, he has **hypertension** that has not been well controlled. When possible, it is desirable to choose drugs that can address multiple issues to minimize adverse effects and drug interactions.

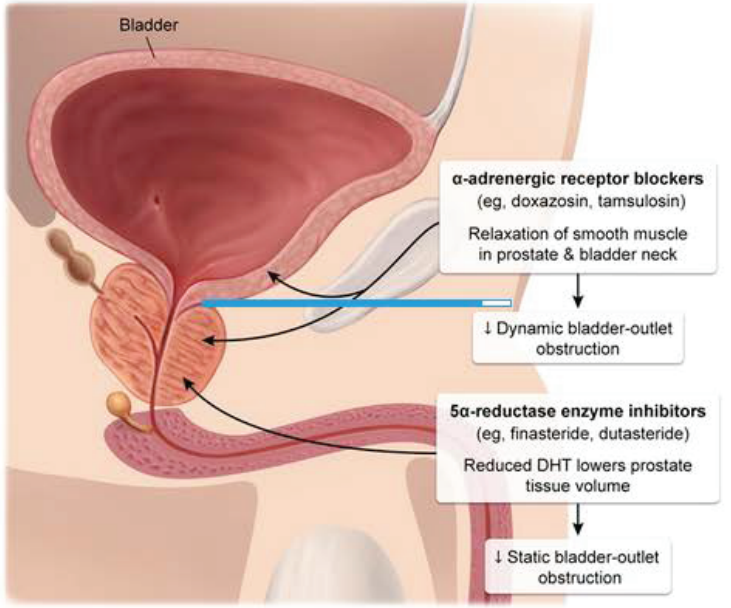
In this patient, an **alpha-1 blocker** (eg, doxazosin, prazosin, terazosin) can be used to **treat both** the BPH symptoms and the hypertension. Although alpha-1 blockers are not first-line medications for hypertension, they can be useful second-line drugs in hypertensive patients with concomitant BPH.

Alpha-1 blockers work by **relaxing smooth muscle** in the bladder neck and prostate, opening up the bladder outlet and decreasing the resistance to the flow of urine. They also relax smooth muscle tone in **arterial walls**, thus decreasing blood pressure. Uroselective alpha-1 blockers (specific for alpha-1A subtype), such as alfuzosin, silodosin, and tamsulosin, affect only the urinary tract smooth muscles; therefore, they would not be helpful in decreasing blood pressure **(Choice F)**.

(Choice B) Finasteride is a 5-alpha-reductase inhibitor that is effective for the treatment of BPH but has no effect on blood pressure. It works by inhibiting the conversion of testosterone to dihydrotestosterone, the hormone that causes progressive glandular enlargement in BPH. After being administered for several months, finasteride decreases the size of the prostate.

Exhibit Display

Benign prostatic hyperplasia (BPH)



DHT = dihydrotestosterone.

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(Choice C) Hydralazine is a powerful, typically third-line antihypertensive that works by relaxing smooth muscles in the arterial walls. It would not be useful in the treatment of BPH.

(Choice D) Hydrochlorothiazide is a thiazide diuretic that functions at the distal convoluted tubule of the nephron to prevent the reabsorption of sodium, chloride and water by blocking a Na/Cl co-transporter. It is one of the first-line medications for the treatment of primary hypertension. Diuretics have no role in the treatment of BPH.

(Choice E) Metoprolol is a selective beta-1-receptor blocker used to treat hypertension and coronary artery disease. It works by blocking adrenergic stimulation of the heart, causing the heart to contract less forcefully and less frequently. Beta-1-receptor blockers would not help with BPH symptoms.

Educational objective:

Alpha-1 blockers such as doxazosin, prazosin, and terazosin are useful for the treatment of both benign

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Educational objective:

Alpha-1 blockers such as doxazosin, prazosin, and terazosin are useful for the treatment of both benign prostatic hyperplasia and hypertension. To minimize adverse effects and drug interactions, it is desirable to prescribe a medication that can address multiple issues at once.

References

- Hypertension

A 32-year-old woman, gravida 2 para 1, with an uncomplicated prenatal course delivered a 4.1-kg (9-lb) newborn at 39 weeks gestation via spontaneous vaginal delivery. Apgar scores were 8 and 10 at 1 and 5 minutes, respectively. Further evaluation in the newborn nursery shows abnormal sexual differentiation. Karyotype analysis shows a 46,XY genotype. Biopsy of gonadal tissue shows a lack of Sertoli cells but normally functioning Leydig cells. Which of the following phenotypes is most likely to be present?

	Internal reproductive organs	External genitalia
A.	Female	Female and Male
B.	Female	Male
C.	Female and Male	Female
D.	Female and Male	Male
E.	Male	Female and Male
F.	Male	Male

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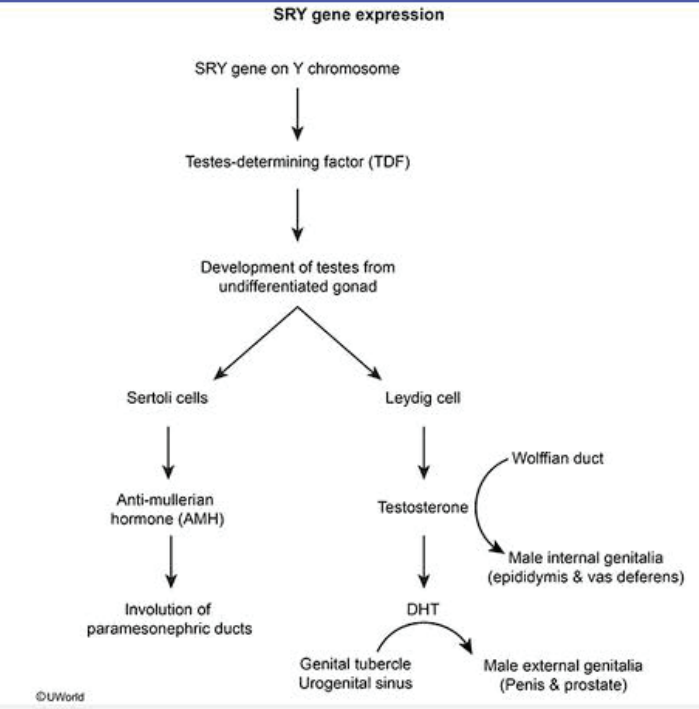
	Internal reproductive organs	External genitalia	
A.	Female	Female and Male	(4%)
B.	Female	Male	(12%)
C.	Female and Male	Female	(6%)
✓ D.	Female and Male	Male	(41%)
E.	Male	Female and Male	(24%)
F.	Male	Male	(9%)

Exhibit Display



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Urogenital sinus (Penis & prostate)

All early embryos have primitive (undifferentiated) gonads, Wolffian (mesonephric) ducts, and Müllerian (paramesonephric) ducts. The primitive gonads develop from the genital ridges and differentiate into either testes (male) or ovaries (female). This differentiation is a result of the **SRY gene** on the Y chromosome that codes for testes-determining factor, which allows XY embryos to **develop testes** from the primitive gonad. In the absence of the Y chromosome, primitive gonads develop into ovaries.

The testes contain both Sertoli and Leydig cells:

1. **Sertoli cells** suppress female internal reproductive organ development by producing **anti-Müllerian hormone** (AMH), which causes **Müllerian duct involution**. Sertoli cells also produce androgen-binding protein, which concentrates testosterone in the seminiferous tubules to enable spermatogenesis.
2. **Leydig cells** secrete testosterone, which stimulates the **Wolffian** (mesonephric) ducts to develop into **internal male** reproductive organs (eg, epididymides, vas deferens, ejaculatory ducts, seminal vesicles). Testosterone is peripherally converted into **dihydrotestosterone**, which transforms the genital tubercle, urogenital folds, and labioscrotal swelling into the **external male** reproductive organs.

In the **absence of Sertoli cells or AMH**, the Müllerian ducts develop into the **internal female** reproductive

genital tubercle, urogenital folds, and labioscrotal swelling into the **external male** reproductive organs.

In the **absence of Sertoli cells or AMH**, the Müllerian ducts develop into the **internal female** reproductive organs (eg, fallopian tubes, uterus, cervix, upper vagina). Therefore, this infant would develop male internal and external reproductive organs due to the presence of Leydig cells **(Choice C)**. The infant would also have female internal reproductive organs from the lack of Sertoli cells.

(Choices A and B) Female internal reproductive organs would develop from a normal XX embryo (or an XY embryo with absence of the SRY gene). The presence of ambiguous or male-type genitalia in genetic females is consistent with androgen excess, as can occur with congenital adrenal hyperplasia due to 21-hydroxylase or 11β-hydroxylase deficiency.

(Choice E) The development of only male internal reproductive organs requires normal functioning of both Sertoli and Leydig cells. Ambiguous (undervirilized) genitalia in genetic males can occur with 17-alpha-hydroxylase deficiency.

(Choice F) Male internal and external reproductive organs are indicative of normal development of an XY embryo with both Sertoli and Leydig cell function.

Educational objective:

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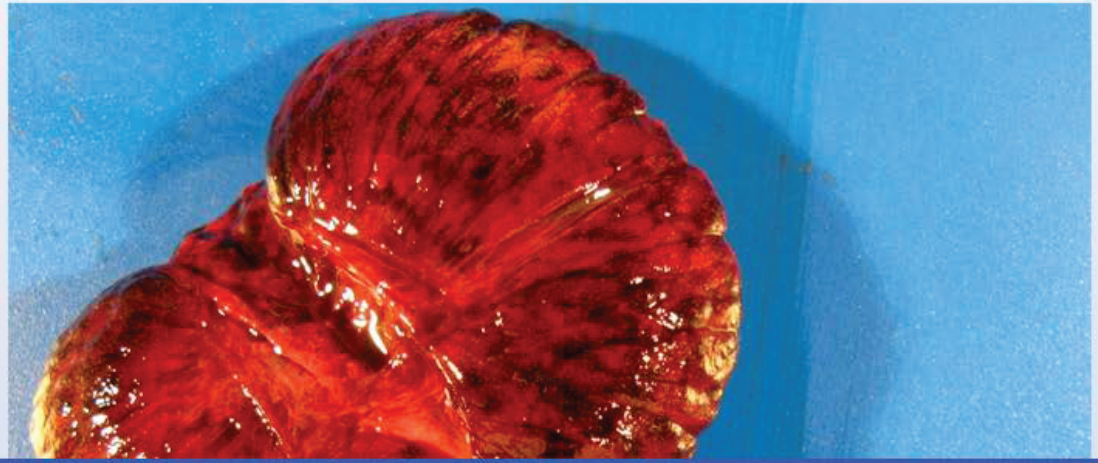
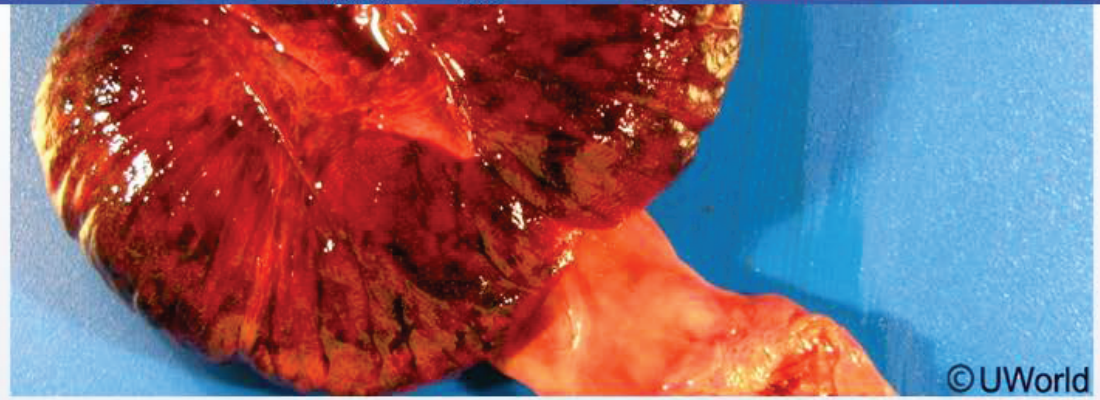
Educational objective:

The SRY gene on the Y chromosome codes for the testes-determining factor, which differentiates the primitive gonads into testes. Sertoli cells produce anti-Müllerian hormone, which causes regression of the Müllerian ducts and suppresses female internal reproductive organ development. Leydig cells produce testosterone, differentiating Wolffian ducts into internal male reproductive organs. Dihydrotestosterone is required for differentiation of the external male genitalia.

References

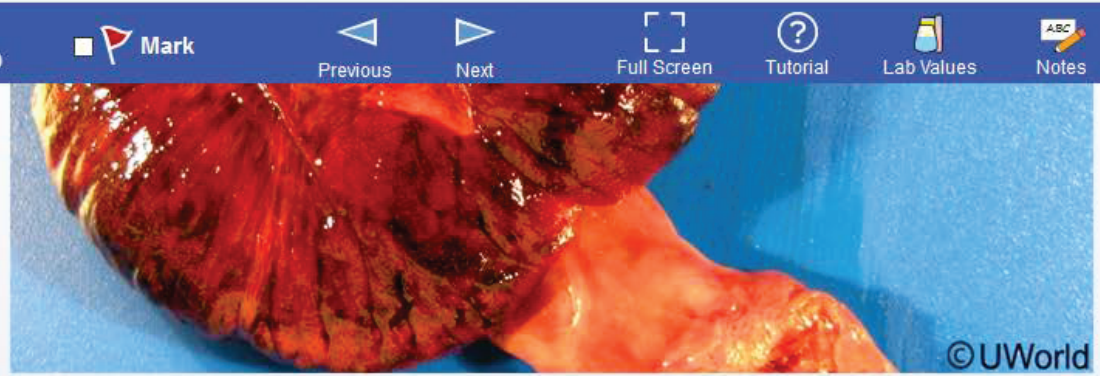
A 16-year-old boy is brought to the emergency department due to severe right groin pain that has worsened over the past 12 hours. During the last month, the patient has had several episodes of mild scrotal pain while walking between classes at school. He has no history of traumatic injury and is sexually active. Medical history is unremarkable except for an inguinal hernia repaired a year ago. Temperature is 36.9 C (98.4 F), blood pressure is 116/78 mm Hg, and pulse is 86/min. On examination, the right hemiscrotum is swollen and tender. The bisected gross specimen from an orchiectomy is shown in the image below.





Which of the following is the most likely mechanism of this patient's acute testicular pain?

A. Abnormal collection of fluid within the scrotum
B. Anatomic defect causing increased mobility of the testis
C. Clonal proliferation of testicular germ cells
D. Migration of bacteria from the urinary tract
E. Postsurgical clotting of the pampiniform plexus



Which of the following is the most likely mechanism of this patient's acute testicular pain?

A. ~~Abnormal collection of fluid within the scrotum~~ (8%)

✓ B. Anatomic defect causing increased mobility of the testis (59%)

C. Clonal proliferation of testicular germ cells (5%)

D. Migration of bacteria from the urinary tract (3%)

E. Postsurgical clotting of the pampiniform plexus (23%)

Correct

59%

01 min, 38 secs

10/05/2020

Testicular torsion	
Pathogenesis	• Twisting of spermatic cord • Venous congestion, hemorrhagic infarction & necrosis of testis • ↑ Risk with poor fixation of testis to tunica vaginalis
Clinical features	• Testicular, inguinal, or abdominal pain • Nausea, vomiting • Examination findings ◦ Swollen, erythematous hemiscrotum ◦ Elevated, horizontally positioned testicle ◦ Absent cremasteric reflex
Imaging	• No testicular blood flow on Doppler ultrasound
Management	• Immediate surgical detorsion

This patient with severe groin pain and unilateral scrotal swelling has evidence of **hemorrhagic infarction** (ie, venous congestion with extravasation of blood) of the testicle, consistent with **testicular torsion**.

This patient with severe groin pain and unilateral scrotal swelling has evidence of **hemorrhagic infarction** (ie, venous congestion with extravasation of blood) of the testicle, consistent with **testicular torsion**.

Testicular torsion is caused by spermatic cord twisting, which most commonly occurs in patients with **inadequate fixation** of the lower pole of the testis to the tunica vaginalis. This **anatomic defect** (ie, bell clapper deformity) allows for **increased mobility of the testis**, which can turn freely within the scrotum. As the testis and cord rotate, the pampiniform plexus becomes compressed, leading to reduced venous outflow and hemorrhagic infarction of the testicle. Diminished testicular perfusion can rapidly progress to ischemia and necrosis.

The classic presentation is an acute onset of **severe scrotal pain** and **swelling** with an elevated, high-riding testis and an absent cremasteric reflex. Groin or lower abdominal pain may be the initial presentation in some, and there may be a history of milder, self-resolving episodes caused by intermittent torsion, as seen in this patient. Emergency surgical detorsion (ideally within 4-6 hr of symptom onset) is required to salvage the testis, but orchiectomy may be necessary if the testicle is necrotic or blood flow cannot be restored.

(Choice A) An abnormal fluid collection between the parietal and viscera tunica vaginalis describes a hydrocele, which causes scrotal swelling but not acute pain.

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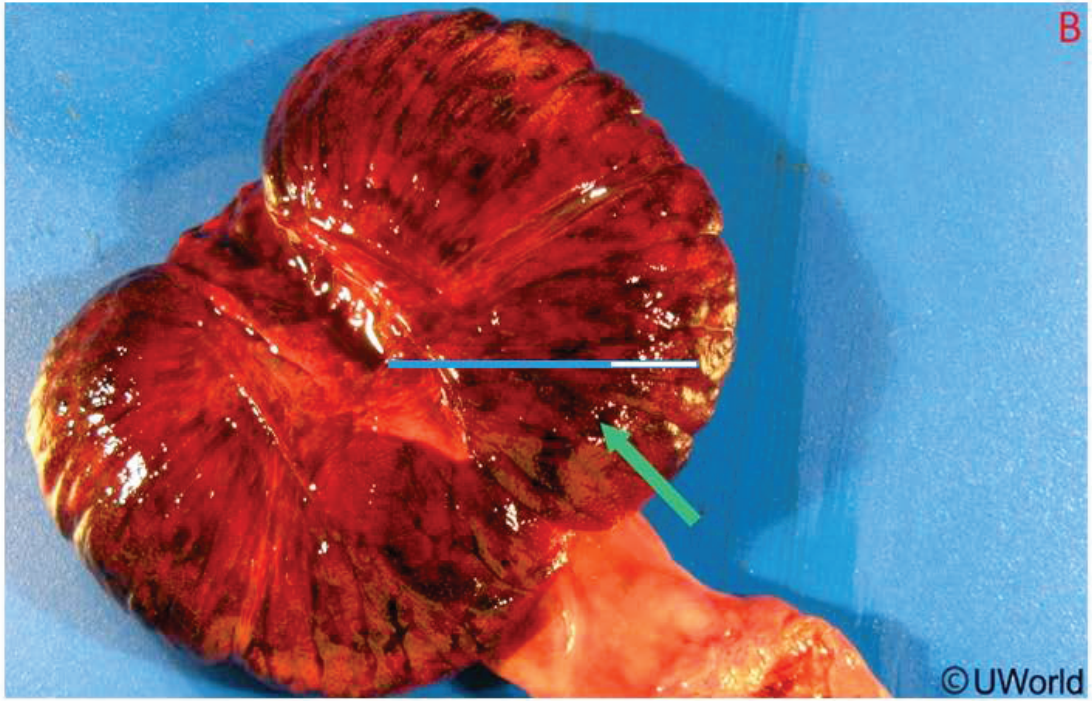

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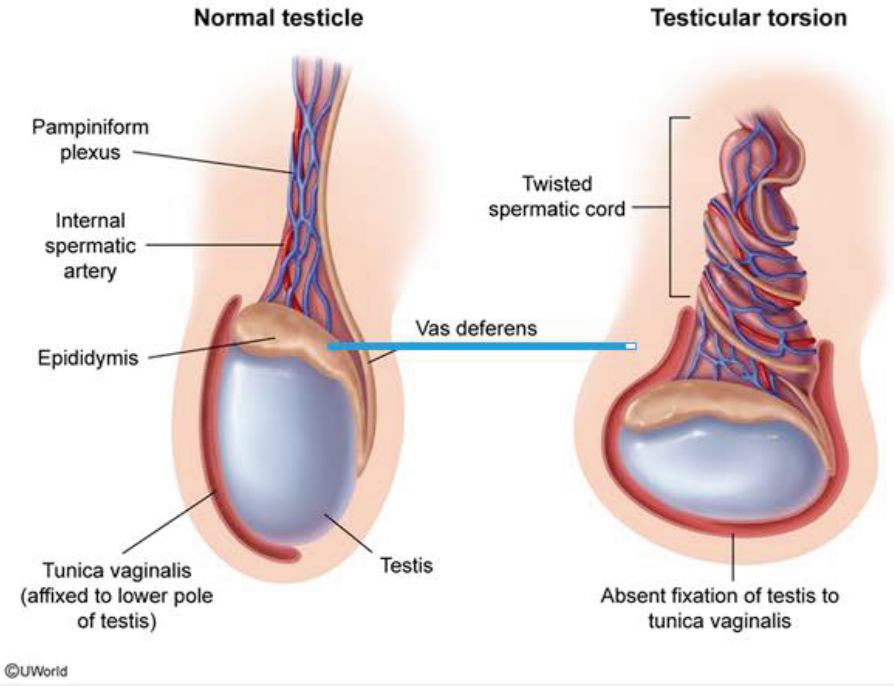

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cannot be restored.

(Choice A) An abnormal fluid collection between the parietal and viscera tunica vaginalis describes a hydrocele, which causes scrotal swelling but not acute pain.

(Choice C) Clonal proliferation of testicular germ cells is seen with a germ cell tumor (eg, seminoma), which most often presents as a nontender testicular mass.

(Choice D) Infection (eg, epididymitis, epididymoorchitis) due to bacterial migration from the urinary tract can cause scrotal pain and swelling, but additional symptoms (eg, fever, dysuria) are often present, and a history of sporadic painful episodes is not typical. Moreover, testicular edema occurs due to inflammation, not hemorrhagic infarction.

(Choice E) Postoperative clotting of the pampiniform plexus (ie, thrombotic varicocele) is a rare surgical complication that causes acute scrotal pain and swelling. However, this patient's inguinal hernia repair was a year ago, making postsurgical complication unlikely.

Educational objective:
Testicular torsion is characterized by spermatic cord twisting due to an anatomic defect that allows increased testicular mobility. The presentation includes severe scrotal pain and swelling due to venous compression and hemorrhagic infarction of the testis.

cannot be restored.

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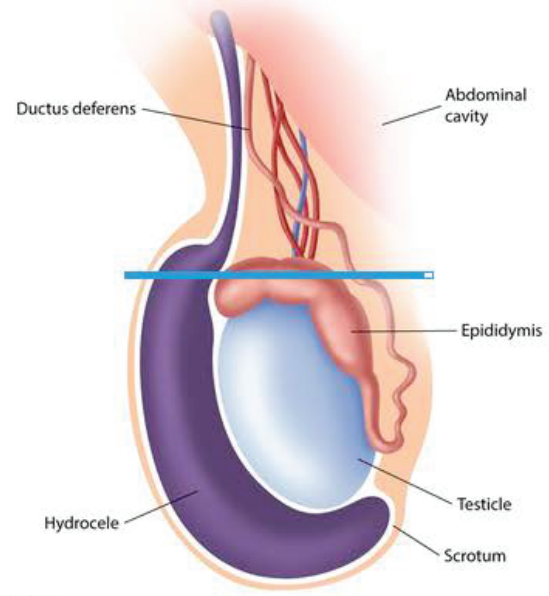
Communicating hydrocele



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A 6-month-old boy is brought to the urology clinic for follow-up of an undescended right testicle discovered during evaluation in the newborn nursery. Physical examination shows absence of a palpable right testis in the scrotal sac. However, a round mass is palpated superior to the scrotum in the inguinal canal. Orchiopexy, the placement and fixation of the testis in the scrotum, is recommended to the family. During this patient's procedure, the malpositioned testis will most likely be pulled through a physiologic opening in which of the following structures?

A. Conjoint tendon
B. External oblique muscle aponeurosis
C. Femoral ring
D. Internal oblique muscle aponeurosis
E. Rectus muscle sheath

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A. Conjoint tendon (5%)
B. External oblique muscle aponeurosis (38%)
C. Femoral ring (16%)
D. Internal oblique muscle aponeurosis (32%)
E. Rectus muscle sheath (7%)

Correct

38%
Answered correctly

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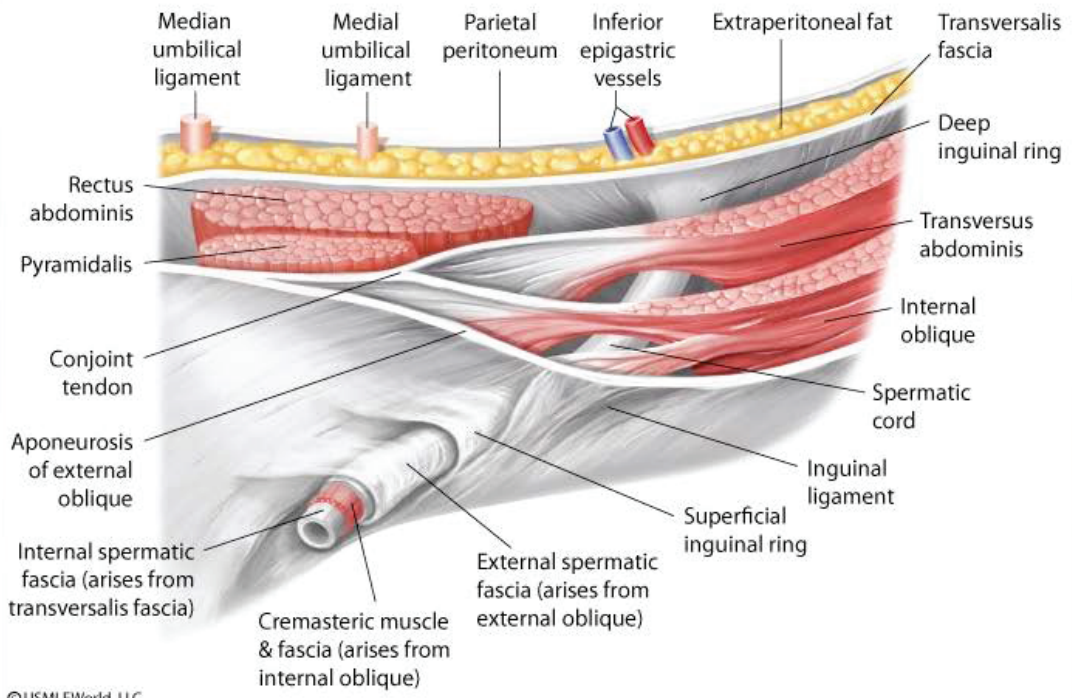
Spermatic cord layers



Testicles develop in the fetal abdomen during organogenesis. Between 8 weeks and full term, each testis

Testicles develop in the fetal abdomen during organogenesis. Between 8 weeks and full term, each testis descends from the abdomen into the inguinal canal through the deep inguinal ring, which is an opening in the transversalis fascia bounded laterally by the transversus abdominis muscle and medially by the inferior epigastric vessels. Each testis then passes anteromedially through the canal and enters the scrotum via the **superficial inguinal ring**, which is a physiologic opening in the **external oblique muscle aponeurosis** above the pubic tubercle.

Cryptorchidism is the failure of one or both testes to descend to the scrotum before birth, which occurs more commonly in preterm neonates. It is associated with a significantly increased risk of **testicular cancer** and **infertility**. A testis that is palpable in the inguinal canal typically descends spontaneously by age 6 months. Testes that have not descended by this point are unlikely to do so and require surgical intervention (ie, **orchiopexy**).

In this case, the patient's undescended testicle is **lodged within the inguinal canal** and must be mobilized through the superficial inguinal ring and stitched into place in the scrotum.

(Choice A) The conjoint tendon is the common tendon of the transversus abdominis and internal oblique muscles. It forms part of the posterior wall of the inguinal canal.

(Choice C) The femoral ring is a physiologic opening between the abdominal cavity and the femoral

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(Choice A) The conjoint tendon is the common tendon of the transversus abdominis and internal oblique muscles. It forms part of the posterior wall of the inguinal canal.

(Choice C) The femoral ring is a physiologic opening between the abdominal cavity and the femoral canal. It transmits lymphatic vessels but not the spermatic cord.

(Choice D) The internal oblique muscle aponeurosis contributes to the formation of the conjoint tendon and rectus muscle sheath. In addition, the cremaster muscle originates from the internal oblique muscle itself.

(Choice E) The rectus muscle sheath is formed by the confluence of the aponeuroses of the external and internal oblique muscles and the transversus abdominis muscle.

Educational objective:
The superficial and deep inguinal rings are physiologic openings in the external abdominal oblique aponeurosis and the transversalis fascia, respectively. Surgical repair of an undescended testicle lodged in the inguinal canal involves moving the testis through the superficial inguinal ring and fixing it in the scrotum (ie, orchiopexy).

Anatomy	Male Reproductive System	Cryptorchidism
Subject	System	Topic

(Choice A) The conjoint tendon is the common tendon of the transversus abdominis and internal oblique

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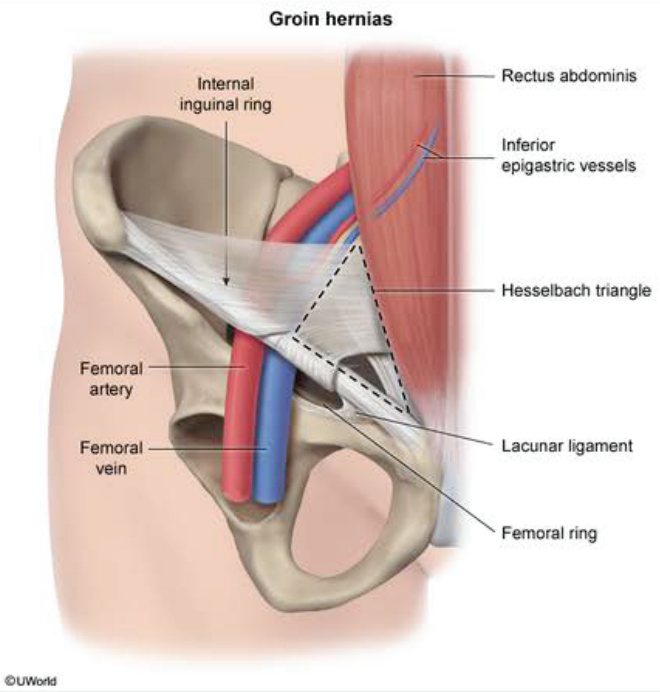

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A 62-year-old man comes to the office due to decreased libido and failure to achieve satisfactory erections. Medical history is notable for coronary artery disease, hypertension, atrial fibrillation, and heart failure with reduced ejection fraction, for which he takes a number of medications. Blood pressure is 110/70 mm Hg and pulse is 70/min. Oxygen saturation on room air is 95%. Examination shows a left ventricular third heart sound and trace pitting ankle edema. Breast examination reveals bilateral breast enlargement with mild tenderness. Which of the following is the most likely cause of this patient's current symptoms?

A. ACE inhibitor
B. Antiplatelet agent
C. Beta-blocker
D. Direct oral anticoagulant
E. Loop diuretic
F. Neprilysin inhibitor
G. Potassium-sparing diuretic

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Medical history is notable for coronary artery disease, hypertension, atrial fibrillation, and heart failure with reduced ejection fraction, for which he takes a number of medications. Blood pressure is 110/70 mm Hg and pulse is 70/min. Oxygen saturation on room air is 95%. Examination shows a left ventricular third heart sound and trace pitting ankle edema. Breast examination reveals bilateral breast enlargement with mild tenderness. Which of the following is the most likely cause of this patient's current symptoms?

A. ACE inhibitor (1%)
B. Antiplatelet agent (0%)
C. Beta-blocker (7%)
D. Direct oral anticoagulant (0%)
E. Loop diuretic (1%)
F. Neprilysin inhibitor (1%)
✓ G. Potassium-sparing diuretic (87%)

Correct

87%
Answered correctly

40 secs
Time Spent

11/03/2020
Last Updated

Medication-induced gynecomastia*	
Drug	**Mechanism**
Estrogens	Direct stimulation of ductal epithelial hyperplasia
Antiandrogens (eg, flutamide, bicalutamide)	Competitive inhibition of testosterone receptor
5-alpha reductase inhibitors (eg, finasteride)	↓ Conversion of testosterone to dihydrotestosterone
Spironolactone	↓ Testosterone synthesis & inhibition of testosterone receptor
Ketoconazole	↓ Synthesis of steroid hormones (↓ androgen > ↓ estrogen)
Cimetidine	Inhibition of testosterone receptor
Androgen-anabolic steroids	Aromatization of androgens to estrogen

*Drugs that increase the estrogen-to-testosterone ratio are associated with gynecomastia.

This patient is most likely being treated with **spironolactone**, an aldosterone antagonist that acts as a **potassium-sparing diuretic**. In patients with **heart failure**, it reduces retention of sodium and water and attenuates the pathologic cardiac remodeling and deterioration in left ventricular function caused by local effects of aldosterone.

However, spironolactone also has prominent antiandrogenic effects due to **blockade of the androgen receptor** and **decreased testosterone** production. **Gynecomastia** is abnormal growth of male breast tissue caused by a decrease in the physiologic androgen-to-estrogen ratio and is a common adverse effect of spironolactone. Other antiandrogenic symptoms may include decreased libido and impotence. Eplerenone, a more selective aldosterone antagonist, has fewer endocrine adverse effects and can be used in place of spironolactone.

(Choices A and F) Neprilysin inhibitors (eg, sacubitril) decrease the breakdown of atrial natriuretic peptide and brain natriuretic peptide, facilitating the effects of these hormones on vasodilation and diuresis. Adverse effects include angioedema because sacubitril also inhibits bradykinin. ACE inhibitors have a similar adverse effect profile but neither of these drug classes affects testosterone metabolism or causes gynecomastia.

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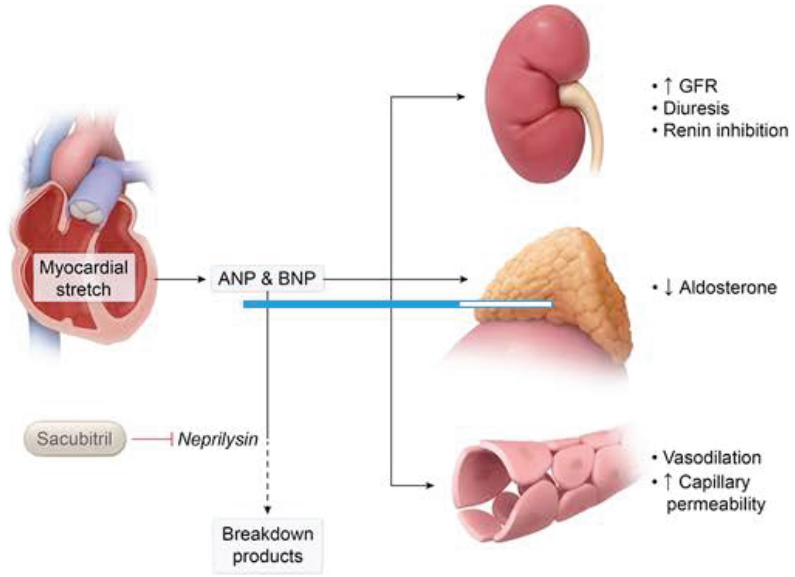
Effects of the natriuretic peptides



ANP = atrial natriuretic peptide; **BNP** = brain natriuretic peptide; **GFR** = glomerular filtration rate.

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gynecomastia

Adverse effects include angioedema because sacubitril also inhibits bradykinin. ACE inhibitors have a similar adverse effect profile but neither of these drug classes affects testosterone metabolism or causes gynecomastia.

(Choices B and D) Antiplatelet agents (eg, aspirin, clopidogrel) and direct oral anticoagulants (eg, apixaban, dabigatran) can cause epistaxis and gastrointestinal bleeding but do not affect androgen metabolism.

(Choice C) Common adverse effects of beta-blockers (eg, carvedilol) include fatigue, hypotension, and bradycardia. They may have a small effect on erectile function but do not affect sex hormone levels or cause gynecomastia.

(Choice E) Loop diuretics (eg, furosemide) reduce edema in patients with heart failure. They can cause hypovolemia, hypotension, and electrolyte abnormalities but do not have a significant antiandrogenic effect.

Educational objective:
Spironolactone is an aldosterone antagonist commonly used to treat heart failure. It has significant antiandrogenic effects and can cause gynecomastia, decreased libido, and impotence. Eplerenone is a more selective aldosterone antagonist with fewer adverse effects.

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A 67-year-old man comes to the office for a routine health maintenance evaluation. He feels well and has no specific symptoms. Vital signs are within normal limits. Digital rectal examination reveals a firm prostatic nodule. The patient undergoes transrectal prostate biopsy, and microscopy reveals sheets of tumor cells infiltrating the stroma with no glandular differentiation; the tumor cells have large vesicular nuclei and prominent nucleoli. Imaging shows enlargement of several iliac lymph nodes. Which of the following is the best description of this patient's tumor?

A. Higher-Gleason score and higher stage
B. Higher-Gleason score and lower-stage
C. Lower-Gleason score and higher-stage
D. Lower-Gleason score and lower-stage

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- A. Higher-Gleason score and higher stage (68%)
- B. Higher-Gleason score and lower-stage (8%)
- C. Lower-Gleason score and higher-stage (21%)
- D. Lower-Gleason score and lower-stage (1%)

Correct

68%
Answered correctly

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Prostate cancer is typically diagnosed by transrectal ultrasound–guided biopsy, which uses ultrasound guidance to take multiple core biopsy samples from random locations within the peripheral zone of the prostate. Subsequent histopathologic examination confirms the presence of cancer and determines the **degree of glandular architecture abnormality**, which is summarized by the **Gleason grade**.

The lowest Gleason grade of 1 is assigned to well-differentiated tumors; these tumors resemble normal prostatic tissue and are generally arranged into small, well-formed, closely packed glands. In contrast, the **highest Gleason grade of 5** is assigned to **poorly differentiated** tumors; these tumors do not resemble normal prostatic tissue and are generally arranged into **sheets of invasive cells** with **no glandular elements**. The 2 predominant Gleason grades in the core biopsies are added together to generate the Gleason score (eg, a tumor that is mostly Gleason grade 3 and 4 would have a Gleason score of 7). The higher the Gleason score, the higher the risk of spread outside of the prostate.

Staging is a marker of **degree of spread** from the site of cancer origin. Low stage is seen in those with disease confined to the prostate; a higher stage is seen in those with regional (eg, lymph node) or metastatic (eg, bone) lesions. In this case, the presence of **enlarged iliac nodes** likely indicates metastases to the regional lymph nodes; therefore, he would have a **higher stage** of disease.

Educational objective:

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Staging is a marker of **degree of spread** from the site of cancer origin. Low stage is seen in those with disease confined to the prostate; a higher stage is seen in those with regional (eg, lymph node) or metastatic (eg, bone) lesions. In this case, the presence of **enlarged iliac nodes** likely indicates metastases to the regional lymph nodes; therefore, he would have a **higher stage** of disease.

Educational objective:
Prostate cancer is graded by Gleason grade, which is a measure of glandular architecture disruption and risk of extra-organ spread; poorly differentiated prostate cancer (eg, no glandular structure) is assigned a high Gleason grade, whereas well-differentiated prostate cancer (eg, well-formed glandular structure) is assigned a low Gleason grade. Staging is a marker of the extent of spread from the primary cancer site; regional lymph node involvement or distant metastases indicate a higher stage of disease.

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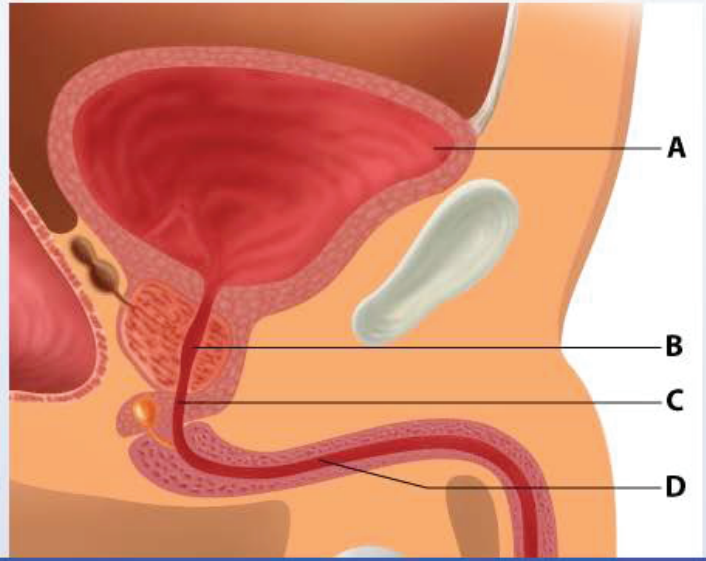
A 45-year-old man is brought to the emergency department after a motor vehicle accident. He is unable to void and complains of a full bladder sensation. Foley catheter placement is attempted, but the procedure is aborted once resistance is encountered and the patient begins complaining of pain. A CT scan of his chest, abdomen, and pelvis shows a left hemothorax and pelvic fracture. This patient is most likely to have an injury involving which of the following portions of the urogenital tract?



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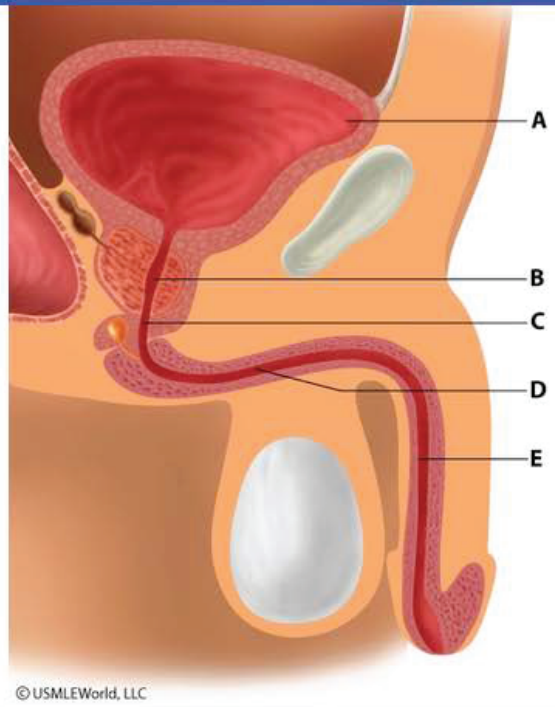

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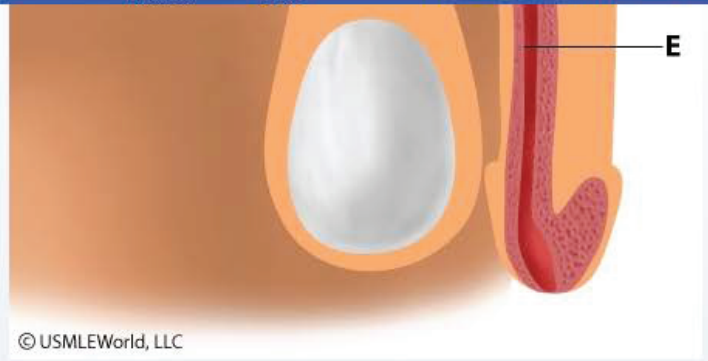

- A.A
- B.B
- C.C
- D.D
- E.E

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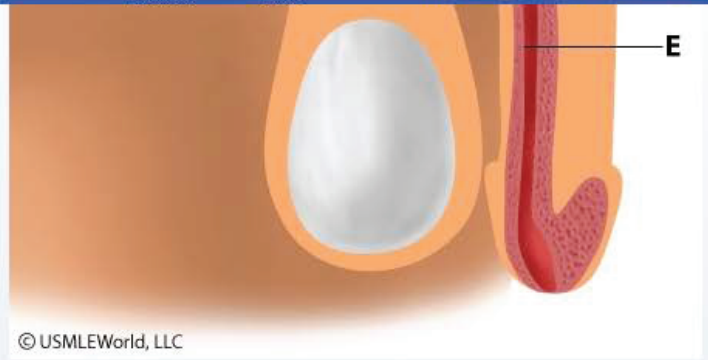

- A. A (6%)
- B. B (17%)
- ✓ C. C (54%)
- D. D (20%)
- E. E (1%)

Correct

54%

43 secs

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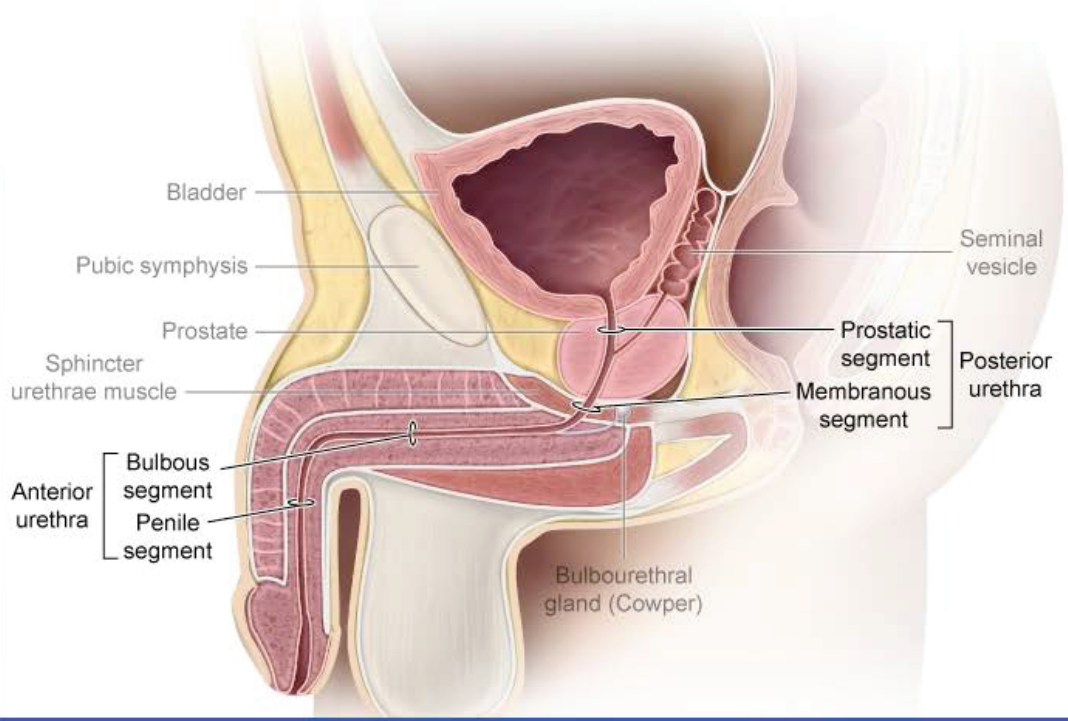
Male urogenital anatomy



The presence of a pelvic fracture and inability to void despite the sensation of a full bladder is suggestive of urethral injury. Additional signs of urethral injury include the presence of blood at the urethral meatus and a high-riding, boggy prostate (caused by hematoma formation below the gland). If urethral injury is suspected, placement of a Foley catheter is contraindicated and should not be attempted as it can worsen the injury; a retrograde urethrogram should be performed first to assess urethral integrity.

Urethral injuries most commonly occur in men because of their longer urethral length and are divided into anterior and posterior urethral injuries. The posterior urethra is located above the bulb of the penis, and the anterior urethra lies within the bulb and the remainder of the corpus spongiosum. The posterior urethra is further divided into the prostatic and membranous segments; the anterior urethra is divided into bulbous and penile segments. In contrast to the prostatic and bulbous segments, the membranous segment is relatively unsupported by the adjacent tissues and is the weakest point of the posterior urethra. Trauma to the pelvis severe enough to cause fracture often results in disruption of the posterior urethra at the bulbomembranous junction.

(Choice A) Injury of the anterior bladder wall is common with pelvic fractures and is usually associated with extraperitoneal leakage of urine. Superior bladder wall ruptures often occur with abdominal trauma when the bladder is full and result in leakage of urine into the intraperitoneal cavity. This patient's full

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(Choice A) Injury of the anterior bladder wall is common with pelvic fractures and is usually associated with extraperitoneal leakage of urine. Superior bladder wall ruptures often occur with abdominal trauma when the bladder is full and result in leakage of urine into the intraperitoneal cavity. This patient's full bladder sensation and inability to pass a Foley catheter makes a urethral injury more likely.

(Choice B) The prostatic urethral segment is strengthened by the surrounding prostate tissue and thus is less likely to be damaged from a pelvic fracture.

(Choice D) Although the bulbous urethral segment is reinforced by the surrounding corpus spongiosum, it is susceptible to crushing injuries when the perineum is struck forcefully (ie, straddle injury). Common mechanisms include falling on the crossbar of a bicycle or the top of a fence.

(Choice E) The penile urethral segment is most commonly injured due to penetrating trauma or instrumentation.

Educational objective:
Injury to the posterior urethra is associated with pelvic fractures, and the anterior urethra is most commonly damaged in straddle injuries. Inability to void with a full bladder sensation, a high-riding boggy prostate, and blood at the urethral meatus are suggestive of urethral injury, particularly in the presence of a pelvic fracture. If urethral injury is suspected, placement of a Foley catheter is contraindicated.

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A 23-year-old man comes to the physician complaining of right-sided testicular swelling. He first noticed the swelling 1 week ago while getting ready for work. He denies any testicular pain or history of trauma. However, he has noticed a heavy, pressing sensation involving his scrotum and lower abdomen. Physical examination reveals asymmetric swelling of the right testis, and subsequent ultrasonography shows a solid testicular mass. If malignant, this patient's tumor is most likely to spread to which of the following lymph node groups?

A. Superficial inguinal
B. Deep inguinal
C. External iliac
D. Common iliac
E. Inferior mesenteric
F. Para-aortic

Submit

A 23-year-old man comes to the physician complaining of right-sided testicular swelling. He first noticed the swelling 1 week ago while getting ready for work. He denies any testicular pain or history of trauma. However, he has noticed a heavy, pressing sensation involving his scrotum and lower abdomen. Physical examination reveals asymmetric swelling of the right testis, and subsequent ultrasonography shows a solid testicular mass. If malignant, this patient's tumor is most likely to spread to which of the following lymph node groups?

A. Superficial inguinal (7%)
B. Deep inguinal (7%)
C. External iliac (1%)
D. Common iliac (1%)
E. Inferior mesenteric (1%)
F. Para-aortic (80%)

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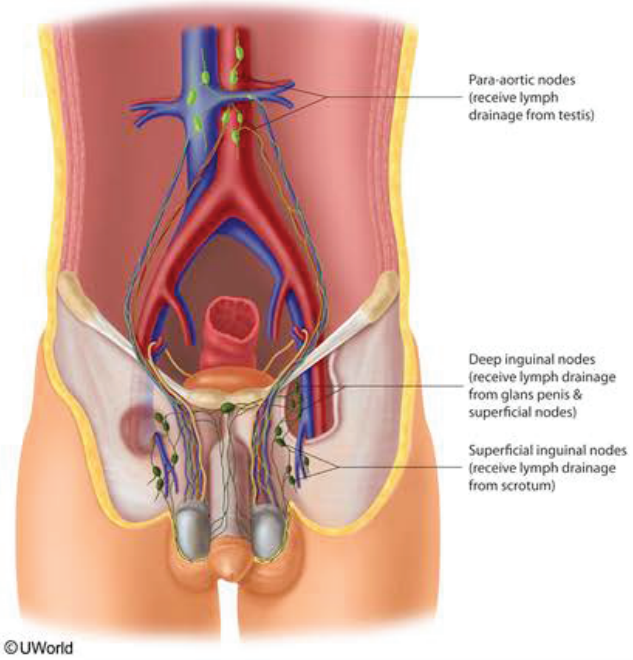
Exhibit Display

Lymph vessels & nodes of male genitalia



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In general, the lymph drainage from a particular organ follows the path of the arterial supply to that site. During fetal development, the testes originate within the retroperitoneum and establish their arterial supply from the abdominal aorta. The testes subsequently descend through the inguinal canals into the scrotum, taking with them their arterial, venous, and lymphatic supplies. Thus, lymph from the testes drains through lymph channels directly back to the para-aortic (retroperitoneal) lymph nodes.

(Choice A) The superficial inguinal lymph nodes are located on the anterior thigh inferior to the inguinal ligament. These nodes drain nearly all cutaneous structures inferior to the umbilicus, including the external genitalia and the anus up to the pectinate line.

(Choice B) The deep inguinal nodes reside under the fascia lata on the medial side of the femoral vein. They receive afferents from the superficial inguinal nodes and deep lymphatic trunks along the femoral vessels. The lymphatics from the glans penis and clitoris also drain directly to these nodes.

(Choice C) The external iliac nodes drain the superficial and deep inguinal nodes and the deep lymphatics of the abdominal wall below the umbilicus.

(Choice D) The common iliac nodes are located alongside the common iliac artery and drain the internal and external iliac nodes

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(Choice B) The deep inguinal nodes reside under the fascia lata on the medial side of the femoral vein. They receive afferents from the superficial inguinal nodes and deep lymphatic trunks along the femoral vessels. The lymphatics from the glans penis and clitoris also drain directly to these nodes.

(Choice C) The external iliac nodes drain the superficial and deep inguinal nodes and the deep lymphatics of the abdominal wall below the umbilicus.

(Choice D) The common iliac nodes are located alongside the common iliac artery and drain the internal and external iliac nodes.

(Choice E) The inferior mesenteric nodes drain the structures supplied with arterial blood by branches of the inferior mesenteric artery (eg, the left colic, sigmoid, and superior rectal arteries). Thus, these nodes drain the descending and sigmoid colon as well as the upper part of the rectum. Their efferents drain to pre-aortic nodes.

Educational objective:
Lymph from the testes drains through lymph channels directly back to the para-aortic lymph nodes. In contrast, lymph from the scrotum drains to the superficial inguinal lymph nodes.

Anatomy	Male Reproductive System	Lymphatic drainage
Subject	System	Topic

A 75-year-old man comes to the office due to 4 weeks of increased urinary hesitancy and progressive low back pain. Spinal imaging reveals multiple lesions suspicious for metastatic cancer. Biopsy of a bone lesion shows well-differentiated adenocarcinoma. Treatment with a medication that does which of the following would most likely reduce the spread of this patient's cancer?

A. Activation of the androgen receptor
B. Activation of the LH receptor
C. Blockade of the estrogen receptor
D. Blockade of the FSH receptor
E. Inhibition of the 17-alpha-hydroxylase enzyme

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A 75-year-old man comes to the office due to 4 weeks of increased urinary hesitancy and progressive low back pain. Spinal imaging reveals multiple lesions suspicious for metastatic cancer. Biopsy of a bone lesion shows well-differentiated adenocarcinoma. Treatment with a medication that does which of the following would most likely reduce the spread of this patient's cancer?

A. ~~Activation of the androgen receptor~~ (9%)
B. ~~Activation of the LH receptor~~ (12%)
C. ~~Blockade of the estrogen receptor~~ (5%)
D. ~~Blockade of the FSH receptor~~ (20%)
E. Inhibition of the 17-alpha-hydroxylase enzyme (52%)

Correct

52%
Answered correctly

01 min, 23 secs
Time Spent

10/17/2020
Last Updated

Explanation

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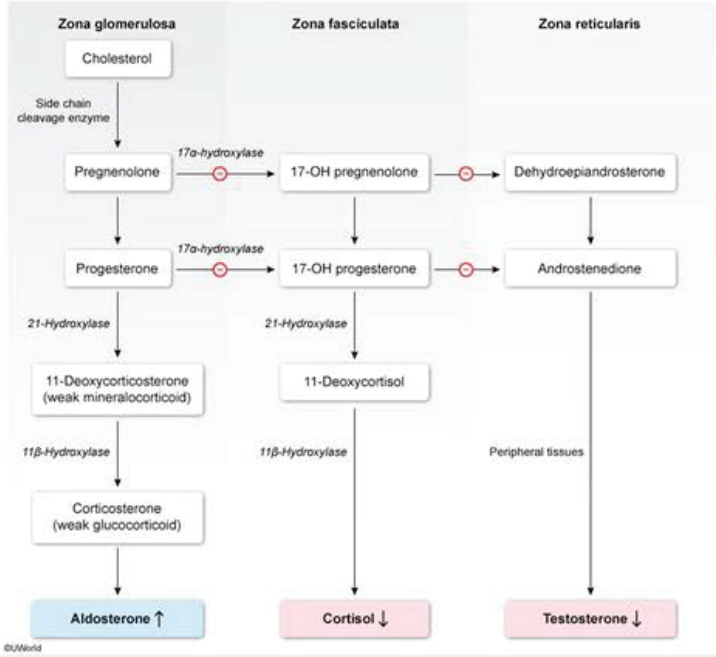
Exhibit Display

Effect of 17α-hydroxylase inhibitors on adrenal steroidogenesis



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Corticosterone

This older patient with urinary hesitancy and multiple bone lesions has biopsy evidence of well-differentiated adenocarcinoma, raising strong suspicion for **metastatic prostate adenocarcinoma**. Prostate cancer is the most common non-skin cancer in men; it has a predilection for metastases to **bone** due to tumor surface proteins that bind to pericytes and bone marrow stromal cells.

Prostate adenocarcinoma is generally an **androgen-sensitive tumor**. Because androgens in men are produced primarily in the testes, initial treatment for advanced disease usually involves medical or surgical orchiectomy to eliminate testicular production of androgens. However, androgens are also produced in the adrenal glands and tumor cells via the expression of **17-alpha-hydroxylase**, a cytochrome P-450 enzyme that converts pregnenolone/progesterone into dehydroepiandrosterone **(DHEA)/androstenedione**. Because these extratesticular androgens can also drive tumor growth, patients with advanced disease and those with castration-resistant prostate cancer generally receive **abiraterone**, a medication that irreversibly **inhibits 17-alpha-hydroxylase**. This limits extratesticular androgen production, which slows the growth of the tumor.

(Choice A) Because prostate cancer is an androgen-sensitive tumor, activation of the androgen receptor would worsen the disease.

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(Choice A) Because prostate cancer is an androgen-sensitive tumor, activation of the androgen receptor would worsen the disease.

(Choice B) LH triggers Leydig cells in the testes to produce androgens. Therefore, activation of the LH receptor would worsen prostate cancer (increased androgen production). Medical orchiectomy involves the administration of GnRH analogues, which reduce LH levels by eliminating the pulsatile stimulation of pituitary gonadotrophs.

(Choice C) Estrogen receptor blockade is used in the treatment of estrogen-sensitive breast and endometrial cancer. Prostate cancer is driven by androgens such as testosterone and DHEA, not estrogen.

(Choice D) FSH induces spermatogenesis in men; LH is responsible for testicular androgen production. Therefore, blockade of FSH would not inhibit systemic androgen generation.

Educational objective:
Patients with advanced or castration-resistant prostate cancer are often treated with an 17-alpha-hydroxylase inhibitors (eg, abiraterone), which block the generation of androgens in the adrenal glands, testes, and tumor cells. This reduces systemic androgen levels, which limit prostate cancer growth.

A 25-year-old man is found to have small testes on physical examination. He has normal male pattern facial and pubic hair. Further laboratory testing reveals a decreased sperm count and normal serum testosterone level. Which of the following is the most likely cause of these findings?

- A. Kallmann syndrome
- B. 5-alpha reductase deficiency
- C. Klinefelter syndrome
- D. Androgen use
- E. Hyperprolactinemia

Submit

A 25-year-old man is found to have small testes on physical examination. He has normal male pattern facial and pubic hair. Further laboratory testing reveals a decreased sperm count and normal serum testosterone level. Which of the following is the most likely cause of these findings?

- A. Kallmann syndrome (6%)
- B. 5-alpha reductase deficiency (11%)
- C. Klinefelter syndrome (14%)
- ✓ D. Androgen use (66%)
- E. Hyperprolactinemia (2%)

Correct

66% Answered correctly

31 secs Time Spent

11/11/2020 Last Updated

Explanation

This patient is taking exogenous **anabolic steroids** (eg, testosterone, synthetic steroidal androgens). Anabolic steroids are utilized by athletes in an effort to increase lean body mass. Adverse effects associated with the excessive use of anabolic steroids include acne, gynecomastia, azoospermia, decreased testicular size and increased aggression. Hypertension, dyslipidemia, cholestatic hepatitis and hepatic failure may also occur.

Serum **testosterone levels** can be low in individuals taking only synthetic androgens (eg, trenbolone), but are **often within the normal range** or elevated due to **exogenous testosterone intake**. Although serum testosterone may appear adequate, lower than normal local testosterone levels in the seminiferous tubules lead to **decreased spermatogenesis**.

(Choice A) Kallmann syndrome is a cause of GnRH deficiency, which results in abnormally low production of sex hormones by the gonads. Affected males present with delayed puberty and an abnormally small penis in addition to other nonsexual findings such as anosmia, hearing loss, and cleft palate.

(Choice B) 5-alpha reductase deficiency results in an inability to convert testosterone to dihydrotestosterone in the peripheral tissues. Affected males are born with ambiguous genitalia. Following puberty, affected patients have normal or elevated levels of serum testosterone.

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penis in addition to other nonsexual findings such as anosmia, hearing loss, and cleft palate.

(Choice B) 5-alpha reductase deficiency results in an inability to convert testosterone to dihydrotestosterone in the peripheral tissues. Affected males are born with ambiguous genitalia. Following puberty, affected patients have normal or elevated levels of serum testosterone.

(Choice C) Klinefelter syndrome (XXY seminiferous tubule dysgenesis) is a common cause of male hypogonadism. Small, firm testes and a decreased serum testosterone level are characteristic. Patients may exhibit diminished secondary sexual characteristics.

(Choice E) Hyperprolactinemia causes hypogonadotropic hypogonadism by suppressing LH and FSH release thereby decreasing serum testosterone in affected males. Symptoms include diminished libido, impotence and oligospermia.

Educational objective:
Adverse effects associated with the use of excessive doses of anabolic steroids include acne, gynecomastia, azoospermia, decreased testicular size, and increased aggression. When measured, serum testosterone is typically normal or elevated. However, endogenous testosterone production and spermatogenesis are decreased.

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A 24-year-old man comes to the emergency department due to a persistent, painful erection that has lasted for more than 8 hours. He had 3 similar episodes in the past 2 years that were less than 30 minutes in duration and resolved with ice packs at home. The patient has had no trauma to the perineal or genital area. He has no other medical conditions and takes no prescription, over-the-counter, or herbal medications. The patient does not use tobacco, alcohol, or illicit drugs. Temperature is 37 C (98.6 F), blood pressure is 124/82 mm Hg, pulse is 84/min, and respirations are 16/min. Examination shows an engorged corpora cavernosa and a rigid, tender penis. The testicles are normal, and the remainder of the examination shows no abnormalities. Penile injection with a medication having which of the following mechanisms would most likely relieve this patient's symptoms?

A. Alpha-1 adrenergic agonism
B. Alpha-1 adrenergic antagonism
C. Beta-1 adrenergic stimulation
D. Beta-2 adrenergic stimulation

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- A. Alpha-1 adrenergic agonism (61%)
- B. Alpha-1 adrenergic antagonism (29%)
- C. Beta-1 adrenergic stimulation (2%)
- D. Beta-2 adrenergic stimulation (6%)

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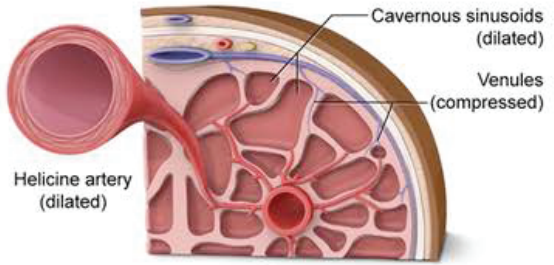
Exhibit Display

Erection and detumescence

↑ Parasympathetic input
↓
Smooth muscle relaxation
↓
↑ Blood flow to the sinusoids
↓
Sinusoid expansion compresses venules
↓
↓ Venous outflow maintains erection



Erect

↑ Sympathetic input
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Smooth muscle contraction
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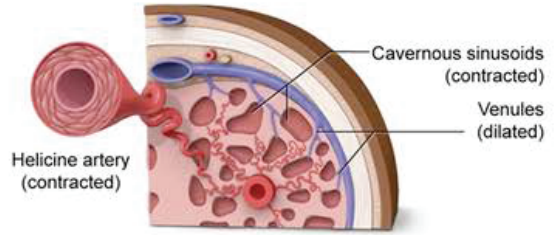
↓ Restored venous outflow* allows penis to return to flaccid state



Flaccid (detumescence)

*Impaired venous outflow (eg, sickle cell disease) can cause a persistent, painful erection (ie, priapism)

Zoom In | Zoom Out | Reset | New | Existing | My Notebook

*Impaired venous outflow (eg, sickle cell disease) can cause a persistent, painful erection (ie, priapism) ©UWorld

The corpora cavernosa of the penis receive sympathetic innervation (T11-L2) via the superior hypogastric plexus and cavernosal nerves.

- In the **flaccid** state, tonic alpha-adrenergic (norepinephrine) **sympathetic** activity maintains high vascular and trabecular smooth muscle tone, preventing the corpora from engorging with blood.
- In an **erection**, activation of **parasympathetic** nerve fibers (S2-S4) induces relaxation of smooth muscle in cavernous arteries and trabeculae. The increased blood flow fills the relaxed corpora, which subsequently causes compression of the emissary veins against the tunica albuginea, blocking the outflow of blood and further increasing pressure within the corpora cavernosa.

This patient has **priapism**, a painful, firm erection in the absence of sexual stimulus or beyond the normal duration of sexual activity. Priapism is usually idiopathic but can be caused by medications or drugs (eg, trazodone, cocaine) or disease states (eg, sickle cell disease) that disrupt the normal outflow of blood from the corpora cavernosa. Treatment usually includes penile injection of an **alpha-adrenergic agonist** (eg, phenylephrine), which **induces contraction of cavernous smooth muscle**; this reduces venous obstruction by the engorged corpora, increasing venous outflow and **promoting detumescence**.

(Choice B) Alpha-1 antagonists (eg, tamsulosin, doxazosin) inhibit tonic sympathetic activity and can

phenylephrine), which **induces contraction of cavernous smooth muscle**; this reduces venous obstruction by the engorged corpora, increasing venous outflow and **promoting detumescence**.

(Choice B) Alpha-1 antagonists (eg, tamsulosin, doxazosin) inhibit tonic sympathetic activity and can trigger priapism.

(Choice C) Beta-1 agonists (eg, dobutamine) are positive inotropic agents that increase stroke volume and cardiac output. This will increase blood flow to the penis and worsen priapism.

(Choice D) Beta-2 agonists induce trabecular smooth muscle relaxation and increase blood flow to the penis, potentially worsening priapism.

Educational objective:
The penile flaccid state is maintained by tonic alpha-adrenergic (norepinephrine) sympathetic activity, causing high vascular and trabecular smooth muscle tone, preventing corporal engorgement with blood. Priapism can be treated with penile injections of an alpha-adrenergic agonist (eg, phenylephrine), which induce smooth muscle contraction, leading to detumescence.

Pharmacology	Male Reproductive System	Priapism
Subject	System	Topic

A newborn boy is found to have micropenis at birth. Genetic analysis identifies a specific mutation in the NR5A1/SF-1 gene that results in selective impairment in Sertoli cell function. The remainder of the hypothalamic-pituitary-gonadal axis is unaffected. The patient undergoes regular follow-up with a pediatric endocrinologist during childhood and has otherwise normal childhood and pubertal development. When he is 16 years old, serum hormone levels are obtained. Which of the following patterns of blood hormone levels are most likely to be seen as a result of this patient's condition?

	Testosterone	Inhibin	FSH	LH
A.	Decreased	Decreased	Decreased	Decreased
B.	Decreased	Normal	Normal	Increased
C.	Normal	Decreased	Increased	Normal
D.	Normal	Increased	Normal	Normal
E.	Normal	Normal	Increased	Normal

Submit

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	Testosterone	Inhibin	FSH	LH	
A.	~~Decreased~~	~~Decreased~~	~~Decreased~~	~~Decreased~~	(3%)
B.	~~Decreased~~	~~Normal~~	~~Normal~~	~~Increased~~	(7%)
✓ C.	Normal	Decreased	Increased	Normal	(81%)
D.	~~Normal~~	~~Increased~~	~~Normal~~	~~Normal~~	(3%)
E.	~~Normal~~	~~Normal~~	~~Increased~~	~~Normal~~	(3%)

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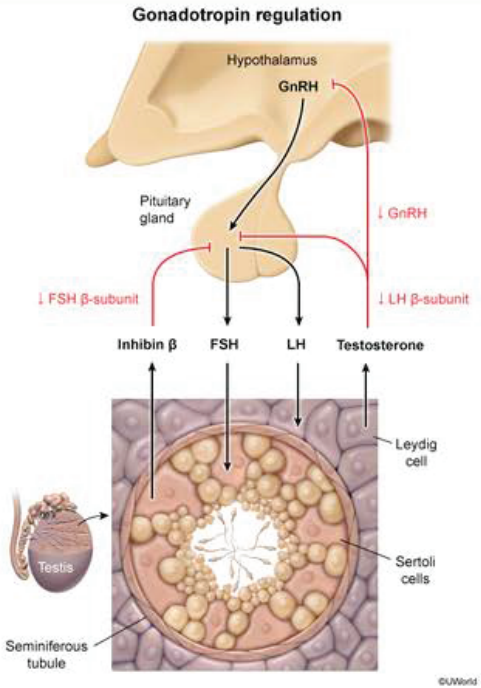

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Sertoli and Leydig cells are the hormone-producing cells of the testis. **Leydig cells**, which are analogous to female theca cells, produce **testosterone** in response to stimulation by **luteinizing hormone**. LH is released from the anterior pituitary in response to gonadotropin-releasing hormone (GnRH) from the hypothalamus. Testosterone causes feedback inhibition of both LH and GnRH release.

Sertoli cells, which are analogous to female granulosa cells, produce the hormone **inhibin** in response to **FSH** from the anterior pituitary. Inhibin suppresses FSH production by the anterior pituitary, although it does not feed back on the hypothalamus. Sertoli cells also facilitate spermatogenesis within the seminiferous tubules.

Steroidogenic factor-1 (SF-1) is a nuclear receptor that regulates the transcription of several genes involved in steroidogenesis, sexual development, and reproduction. Mutations of SF-1/NR5A1 cause a wide variety of phenotypic features in males and females, including genital malformations and Sertoli cell failure. Selective impairment in Sertoli cell function would cause decreased production of inhibin and lead to increased FSH levels **(Choice D)**, as well as infertility due to impaired sperm production. However, the Leydig cells are unaffected, so no changes in testosterone or LH levels would be expected.

(Choice A) Decreased release of all of these hormones is a sign of anterior pituitary failure, which can occur with Kallmann syndrome, sellar mass lesions, pituitary apoplexy, or radiation injury.

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(Choice A) Decreased release of all of these hormones is a sign of anterior pituitary failure, which can occur with Kallmann syndrome, sellar mass lesions, pituitary apoplexy, or radiation injury.

(Choice B) This pattern would be observed if the Leydig cells were selectively impaired. Isolated Leydig cell failure has been reported in patients with LH/hCG receptor defects on Leydig cells.

(Choice E) Most pituitary adenomas arising from gonadotrophs produce only the biologically inactive alpha subunit (nonfunctioning adenomas), although adenomas producing intact FSH are occasionally seen. Inhibin levels may be either normal or elevated. Males with FSH-secreting adenomas are usually asymptomatic, but some will have enlargement of the testes.

Educational objective:
Sertoli cells produce inhibin in response to FSH from the anterior pituitary. Inhibin suppresses FSH production in the pituitary. Sertoli cells also facilitate spermatogenesis within the seminiferous tubules. Impaired Sertoli cell function would lead to decreased production of inhibin, increased FSH levels, and impaired fertility.

References

- Predominant Sertoli cell deficiency in a 46,XY disorders of sex development patient with a new

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An 18-year-old man comes to the office due to 2 days of right testicular pain. The pain is constant and exacerbated by movement. Vital signs are within normal limits. On physical examination, there is swelling and tenderness to palpation localized only to the posterior and superior areas of the right testis. The left testis is normal. Cremasteric reflexes are intact bilaterally. Urinalysis shows numerous leukocytes but no bacteria. Which of the following factors most likely contributed to this patient's current condition?

A. Inadequate childhood vaccination
B. Increased gonadal venous pressure
C. Lack of normal testicular fixation
D. Unprotected sexual intercourse
E. Urethral colonization by coliforms

Submit

An 18-year-old man comes to the office due to 2 days of right testicular pain. The pain is constant and exacerbated by movement. Vital signs are within normal limits. On physical examination, there is swelling and tenderness to palpation localized only to the posterior and superior areas of the right testis. The left testis is normal. Cremasteric reflexes are intact bilaterally. Urinalysis shows numerous leukocytes but no bacteria. Which of the following factors most likely contributed to this patient's current condition?

- ✗ A. Inadequate childhood vaccination (17%)
- B. ~~Increased gonadal venous pressure~~ (11%)
- C. ~~Lack of normal testicular fixation~~ (11%)
- ✓ D. Unprotected sexual intercourse (53%)
- E. ~~Urethral colonization by coliforms~~ (5%)

Incorrect
Correct answer
D

53%
Answered correctly

01 min, 14 secs
Time Spent

09/10/2020
Last Updated

Acute epididymitis	
Epidemiology	• Age <35: **sexually transmitted** (chlamydia, gonorrhea) • Age >35: bladder outlet obstruction (**coliform bacteria**)
Symptoms	• Unilateral testicular **pain** • Epididymal **edema** • Dysuria, frequency (with coliform infection)
Diagnosis	• NAAT for chlamydia and gonorrhea • Urinalysis/culture

NAAT = nucleic acid amplification test; **STI** = sexually transmitted infection.

This patient's acute testicular pain, **posterior testicle tenderness**, and pyuria raises suspicion for **acute epididymitis**. Most cases occur when genitourinary pathogens travel in a retrograde fashion from the urethra via the ejaculatory duct to the vas deferens. The most likely underlying organism can often be inferred based upon the age of the patient:

- Young men (age <35) usually develop acute epididymitis due to ***Chlamydia trachomatis*** or ***Neisseria***

- Young men (age <35) usually develop acute epididymitis due to ***Chlamydia trachomatis*** or ***Neisseria gonorrhoeae***, sexually transmitted pathogens acquired during **unprotected sexual intercourse**. Although these organisms often cause asymptomatic urethritis (no dysuria), **pyuria** is typically seen on urinalysis. Nucleic acid amplification testing is required for diagnosis because urine culture is generally negative.

- Older men (age >35) are less likely to have sexually transmitted infections due to fewer sexual partners and increased rates of monogamy. Acute epididymitis in these patients is generally due to gram-negative colonic flora (eg, *Escherichia coli*), which contaminate the urethra, ascend into the urinary system, and subsequently invade the ejaculatory duct and vas deferens. Most cases arise in the setting of urethral obstruction (eg, benign prostatic hypertrophy) and are characterized by urinary tract symptoms (eg, dysuria, urinary frequency), bacteruria on urinalysis, and positive urine culture **(Choice E)**.

(Choice A) Mumps can occur in those who did not receive appropriate childhood vaccinations and usually presents with a nonspecific prodrome (fever, malaise, myalgias) followed by parotitis. Complications include orchitis, with high fever and severe diffuse testicular pain, which are not seen in this patient.

(Choice B) Varicocele is characterized by distension of the pampiniform plexus due to elevated gonadal

(Choice A) Mumps can occur in those who did not receive appropriate childhood vaccinations and usually presents with a nonspecific prodrome (fever, malaise, myalgias) followed by parotitis. Complications include orchitis, with high fever and severe diffuse testicular pain, which are not seen in this patient.

(Choice B) Varicocele is characterized by distension of the pampiniform plexus due to elevated gonadal venous pressure. It presents as a soft scrotal mass that feels like a "bag of worms" on palpation. Pain is mild or absent.

(Choice C) Testicular torsion is the result of inadequate fixation of the lower pole of the testis to the tunica vaginalis. It is usually characterized by sudden-onset, severe, unilateral testicular pain; nausea; a high-riding testis; and loss of the cremasteric reflex (elevation of testis on pinching of the skin at the upper thigh).

Educational objective:
Epididymitis presents with acute testicular pain, tenderness, and pyuria. It is caused by retrograde passage of organisms from the urethra into the ejaculatory duct and vas deferens. The microbiology is largely influenced by patient age: epididymitis in young men is usually due to sexually acquired infections (eg, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*), whereas in older men (age >35) it is usually due to gram-negative colonic flora.

A 27-year-old Caucasian man comes to the physician with his wife for an infertility evaluation. They have been trying to conceive for the last 14 months without success. A semen analysis shows a normal sperm count but completely immobile sperm due to abnormal tail function. Which of the following additional findings is most likely associated with this patient's condition?

- A. Cleft lip
- B. Coarctation of the aorta
- C. Fat malabsorption
- D. Hypertrophic cardiomyopathy
- E. Liver cirrhosis
- F. Persistent bronchial dilation

Submit

A 27-year-old Caucasian man comes to the physician with his wife for an infertility evaluation. They have been trying to conceive for the last 14 months without success. A semen analysis shows a normal sperm count but completely immobile sperm due to abnormal tail function. Which of the following additional findings is most likely associated with this patient's condition?

A. Cleft lip (2%)
B. Coarctation of the aorta (3%)
C. Fat malabsorption (17%)
D. Hypertrophic cardiomyopathy (3%)
E. Liver cirrhosis (1%)
F. Persistent bronchial dilation (72%)

Correct

72% Answered correctly

34 secs Time Spent

02/20/2021 Last Updated

The finding of **impaired sperm motility** raises concern for **primary ciliary dyskinesia** (PCD), an autosomal recessive condition caused by a variety of mutations in genes responsible for normal flagellar and ciliary function. The clinical manifestations of PCD include:

1. Predisposition to upper and lower respiratory tract infections due to impaired mucociliary clearance. Patients develop chronic cough, **chronic sinusitis**, recurrent otitis media, and bronchiectasis (permanent abnormal airway enlargement).
2. Randomization of left-right body asymmetry; half of all patients have **situs inversus** (reversed right/left positioning of internal organs)
3. **Infertility** due to impaired function of sperm flagella (men) and immobility of fallopian tube cilia (women).

Patients with the triad of situs inversus, chronic sinusitis, and bronchiectasis are said to have **Kartagener syndrome**.

(Choice A) A cleft lip results from failure of the maxillary and medial nasal processes to fuse during development. It is not associated with defects in ciliary structure or function.

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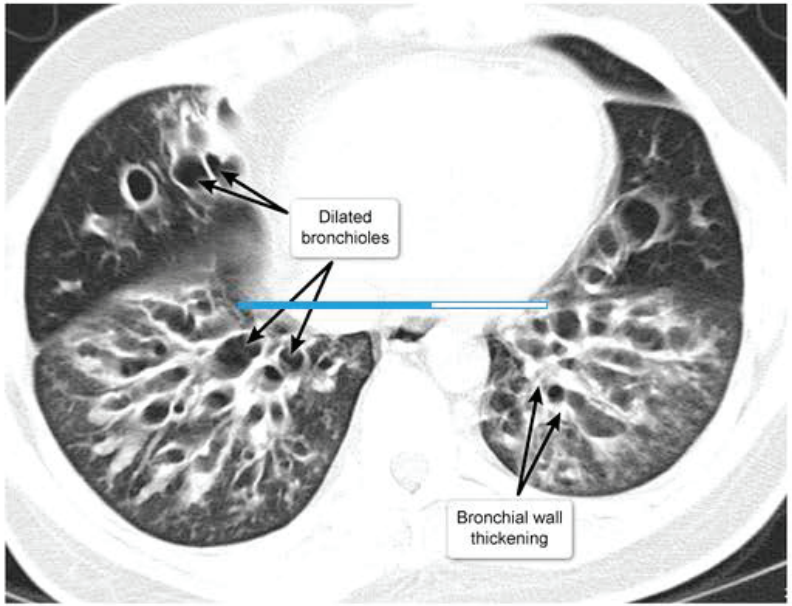
Exhibit Display

Bronchiectasis



Commonly seen in patients with cystic fibrosis

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(Choice A) A cleft lip results from failure of the maxillary and medial nasal processes to fuse during development. It is not associated with defects in ciliary structure or function.

(Choice B) Coarctation of the aorta may be seen in Turner (XO) syndrome.

(Choice C) Fat malabsorption can occur in cystic fibrosis due to pancreatic insufficiency. Although male patients with cystic fibrosis are typically infertile, this results from bilateral absence of the vas deferens (azoospermia) as opposed to the impaired sperm motility seen in Kartagener syndrome.

(Choice D) Most cases of hypertrophic cardiomyopathy are due to mutations in the genes encoding cardiac sarcomere proteins.

(Choice E) Cirrhosis of the liver is not associated with PCD.

Educational objective:
Primary ciliary dyskinesia results from an autosomal recessive mutation in the proteins responsible for normal flagellar and ciliary structure and function (eg, dynein, assembly proteins). Clinical manifestations include situs inversus, chronic sinusitis, bronchiectasis, and infertility.

Pathology Male Reproductive System Bronchiectasis

A 29-year-old man comes to the office due to increased sweating, heat intolerance, insomnia, and unintentional weight loss over the past 4 weeks. The patient has also noticed that his right testis feels bigger than the left but has had no scrotal pain. He has no prior medical problems and takes no medications. The patient does not use tobacco, alcohol, or illicit drugs. Blood pressure is 121/71 mm Hg and pulse is 108/min. On examination, the thyroid is mildly enlarged. Testicular examination reveals an enlarged, nontender right testicle. Laboratory testing shows elevated serum thyroxine and triiodothyronine levels. Scrotal ultrasonography demonstrates a hypoechoic mass within the right testicle. Elevated levels of which of the following substances would most likely explain this patient's symptoms?

A. Alpha-fetoprotein
B. Follicle-stimulating hormone
C. Human chorionic gonadotropin
D. Lactate dehydrogenase
E. Placenta-like alkaline phosphatase

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A. Alpha-fetoprotein (10%)
B. Follicle-stimulating hormone (19%)
C. Human chorionic gonadotropin (61%)
D. Lactate dehydrogenase (4%)
E. Placenta-like alkaline phosphatase (3%)

Correct
61%
01 min, 03 secs
08/29/2020

Common serum tumor markers	
Marker	**Tumor associations**
Alpha-fetoprotein	• Hepatocellular carcinoma • Germ cell
CA 19-9	• Pancreatic
CA 125	• Ovarian
Carcinoembryonic antigen	• Gastrointestinal (eg, colorectal)
Human chorionic gonadotropin	• Choriocarcinoma • Germ cell
Prostate-specific antigen	• Prostate

The human glycoprotein hormone family includes 4 hormones: hCG, TSH, FSH, and LH. Each is a

antigen	

The human glycoprotein hormone family includes 4 hormones: hCG, TSH, FSH, and LH. Each is a heterodimeric structure consisting of an identical alpha subunit noncovalently associated with a unique but homologous beta subunit, which confers its specific biologic properties. The beta subunits of **hCG and TSH share significant sequence homology**; this structural similarity allows hCG to bind and activate the TSH receptor, albeit with much lower affinity than TSH.

hCG is normally produced in the placenta but can also be released by a number of malignancies, especially **choriocarcinoma** and nonseminomatous **germ cell tumors**. This patient likely has a testicular germ cell tumor producing large quantities of hCG. Activation of TSH receptors on the thyroid gland by high levels of hCG can cause **paraneoplastic hyperthyroidism**, presenting with weight loss, sweating, and heat intolerance.

(Choice A) Alpha-fetoprotein can be used as a tumor marker for a number of malignancies, including hepatocellular carcinoma and nonseminomatous germ cell tumors of the testes. However, elevated levels would not result in symptoms of hyperthyroidism.

(Choice B) FSH is produced by gonadotrophs in the anterior pituitary cells. It is not a marker for testicular tumors and has no affinity for thyroid receptors.

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(Choice B) FSH is produced by gonadotrophs in the anterior pituitary cells. It is not a marker for testicular tumors and has no affinity for thyroid receptors.

(Choice D) Lactate dehydrogenase is an enzyme involved in anaerobic glycolysis. Although increased levels can occur with both seminomatous and nonseminomatous tumors of the testes, this enzyme does not interact with TSH receptors.

(Choice E) The majority of circulating alkaline phosphatase comes from bone, liver, gastrointestinal tract, and placenta. Placenta-like alkaline phosphatase is a nonspecific tumor marker that can be increased in testicular seminoma and other malignancies but has no homology with TSH.

Educational objective:
Human chorionic gonadotropin (hCG) has a structure similar to TSH. Patients with testicular germ cell tumors or gestational trophoblastic disease may develop very high serum hCG concentrations, which can stimulate TSH receptors and cause paraneoplastic hyperthyroidism.

References

A 21-year-old previously healthy man comes to the emergency department with acute onset of severe left scrotal pain and nausea. The pain started after he returned home from the gym following an intense workout. He denies any trauma, fever, or dysuria. Examination shows a swollen and tender left testis that lies higher than the right testis. Doppler ultrasound shows decreased arterial blood flow in the left spermatic cord entering the testis. Which of the following is the likely origin of the artery involved in this patient's condition?

A. Abdominal aorta
B. External iliac artery
C. Internal iliac artery
D. Internal pudendal artery
E. Obturator artery
F. Renal artery

Submit

A 21-year-old previously healthy man comes to the emergency department with acute onset of severe left scrotal pain and nausea. The pain started after he returned home from the gym following an intense workout. He denies any trauma, fever, or dysuria. Examination shows a swollen and tender left testis that lies higher than the right testis. Doppler ultrasound shows decreased arterial blood flow in the left spermatic cord entering the testis. Which of the following is the likely origin of the artery involved in this patient's condition?

- A. Abdominal aorta (47%)
- B. External iliac artery (2%)
- C. Internal iliac artery (16%)
- D. Internal pudendal artery (6%)
- E. Obturator artery (0%)
- F. Renal artery (27%)

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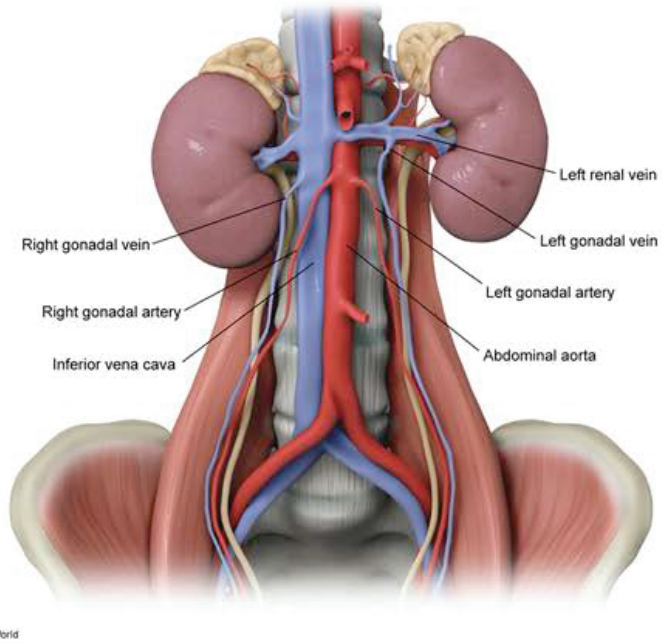
Exhibit Display

Gonadal vasculature



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The **gonadal arteries** arise from the **abdominal aorta** slightly below the renal arteries. Each gonadal artery courses obliquely downward and laterally within the retroperitoneal space near the psoas major muscle. After crossing anteriorly over the ureter, the gonadal arteries run parallel to the external iliac vessels and eventually traverse the inguinal canal to supply the testes via the spermatic cord in males.

This patient most likely has testicular torsion, which is usually due to inadequate fixation of the lower pole of the testis to the tunica vaginalis. Testicular torsion is caused by twisting of the spermatic cord, resulting in compression of the pampiniform plexus of the testicular vein and reduced venous outflow. Arterial blood flow in the testicular arteries is initially preserved or slightly decreased, leading to engorgement and eventual **hemorrhagic infarction**. Torsion is characterized by **acute, severe pain** with nausea/vomiting, an asymmetrically **high-riding testis**, and absent cremasteric reflex (elevation of testis while pinching the skin in upper thigh).

(Choices B and C) The external and internal iliac arteries arise from the common iliac artery. The external iliac artery travels underneath the inguinal ligament and becomes the femoral artery, which supplies the lower extremity. The internal iliac artery provides blood supply to the pelvic wall/viscera, buttock, female reproductive organs, bladder, and medial thigh.

(Choice D) The internal pudendal artery is a branch of the internal iliac artery and provides blood supply to

(Choice D) The internal pudendal artery is a branch of the internal iliac artery and provides blood supply to the anal canal, scrotum, and penis. However, it does not provide blood supply to the testis.

(Choice E) The obturator artery arises from the internal iliac artery and provides blood supply to the pelvis, bladder, and parts of the femoral head and medial thigh muscles.

(Choice F) The renal artery provides blood supply to the kidney. Branches of the renal artery supply the ureter but do not travel to the testis. Unlike the gonadal arteries, the gonadal veins arise from different structures. The right gonadal vein drains directly into the inferior vena cava while the left gonadal vein drains into the left renal vein.

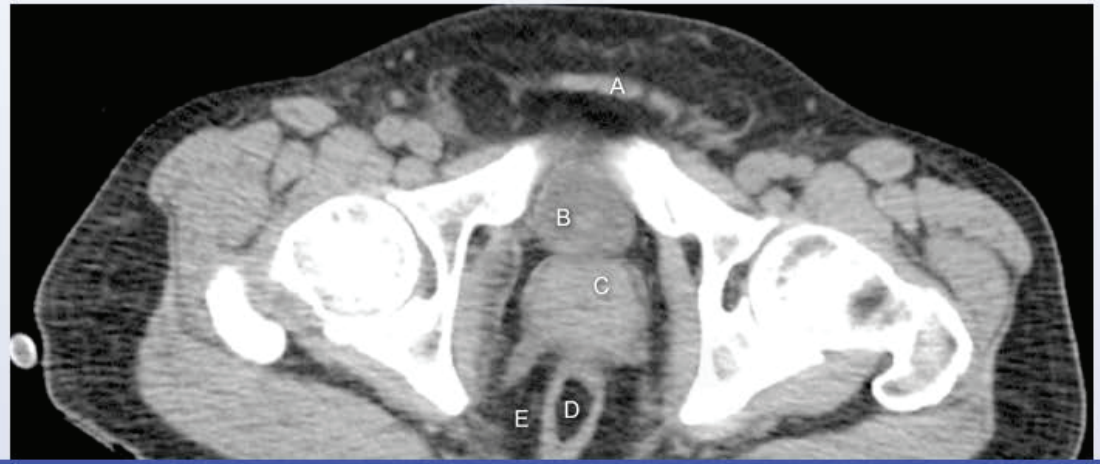
Educational objective:

Testicular torsion is due to twisting of the testis around the spermatic cord (containing the gonadal artery), which can eventually lead to ischemia. The gonadal arteries arise from the abdominal aorta. The right gonadal vein drains directly into the inferior vena cava while the left gonadal vein drains into the left renal vein.

References

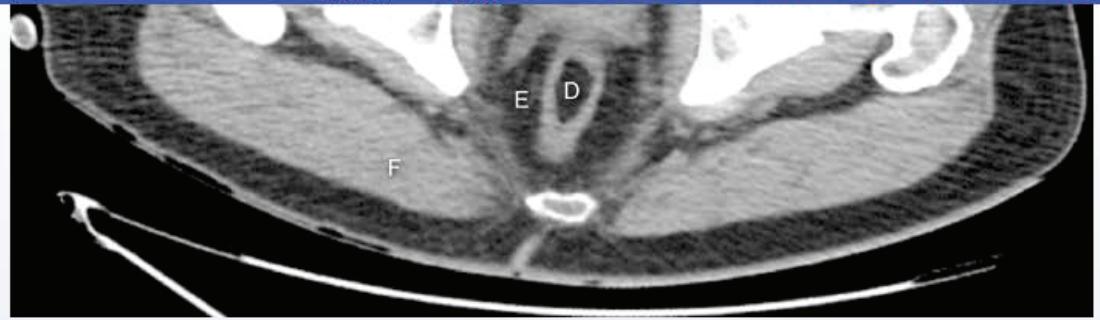
- Testicular torsion: diagnosis, evaluation, and management.

A 63-year-old man comes to the office due to poor urine flow for several months. The patient says that it takes about 10 seconds to initiate a urinary stream. He also needs to strain when urinating or the stream just stops before his bladder is empty. He has tried behavioral modifications, but the symptoms continue to be bothersome. The patient takes lisinopril for hypertension. He has smoked a pack of cigarettes a day for 30 years. His father had urothelial cancer of the bladder. He reports significant improvement several months after starting finasteride. A therapeutic effect on which of the following structures is most likely responsible for this patient's symptomatic improvement?



months after starting finasteride. A therapeutic effect on which of the following structures is most likely responsible for this patient's symptomatic improvement?

- A. A
- B. B



- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

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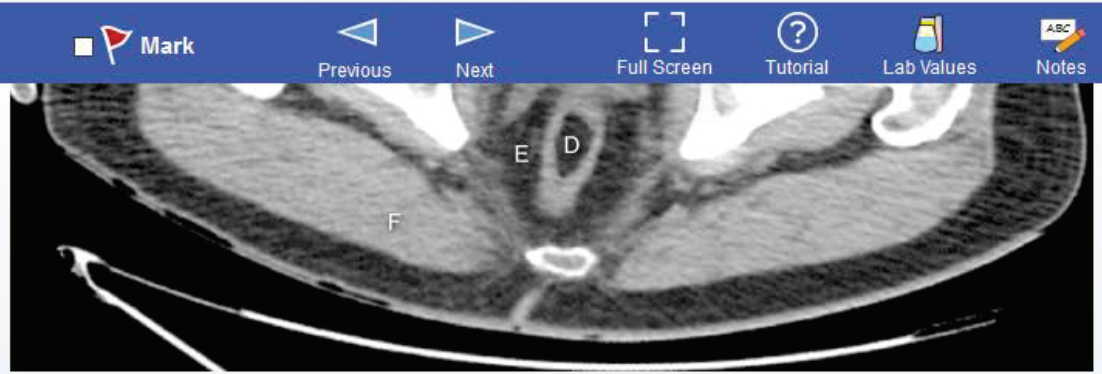

- A.A (1%)
- B.B (24%)
- ✓ C.C (64%)
- D.D (4%)
- E.E (4%)
- F. F (0%)

Correct

64%

17 secs

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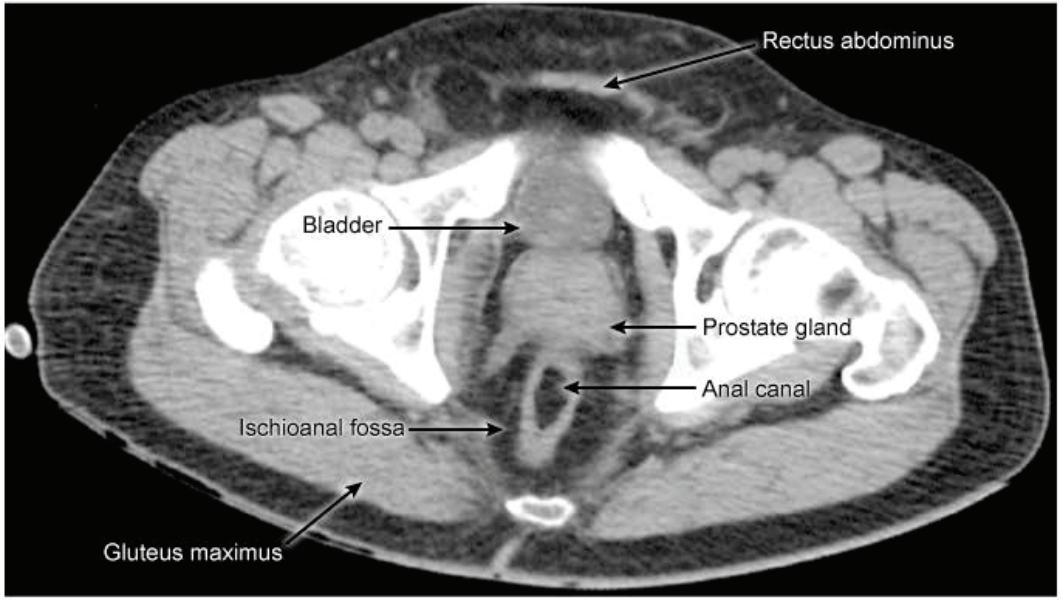
Prostatic hyperplasia



This patient has signs of bladder outlet obstruction (eg, urinary hesitancy, need to strain) most likely due to **benign prostatic hyperplasia** (BPH), a condition that is present in >90% of men age ≥80. The diagnosis

This patient has signs of bladder outlet obstruction (eg, urinary hesitancy, need to strain) most likely due to **benign prostatic hyperplasia** (BPH), a condition that is present in >90% of men age ≥80. The diagnosis is based on history of urinary symptoms and digital rectal examination showing a smooth, homogenously enlarged prostate. The **prostate** is located just anterior to the anal canal **(Choice D)** and posterior to the symphysis pubis (the above CT image is just superior to the joining of the left and right pubic bones).

BPH may cause static urinary obstruction (androgen-mediated enlargement of the prostate) or dynamic obstruction (prostate smooth muscle contraction via α-adrenoceptors). **5-α reductase inhibitors** (eg, finasteride) inhibit the action of androgens on the prostate gland, preventing the conversion of testosterone to dihydrotestosterone and thereby limiting further prostate enlargement. **α-adrenergic blockers** (eg, tamsulosin) relax the smooth muscle in the bladder neck and prostate gland and are also used to control symptoms of BPH.

(Choice B) The distal end of the anterior bladder wall may or may not be visible at this level depending on patient positioning and bladder filling.

Educational objective:

The prostate is located between the pubic symphysis and the anal canal and is visible on inferior sections of the pelvis on CT scan. Benign prostatic hyperplasia is a common, age-related condition that causes

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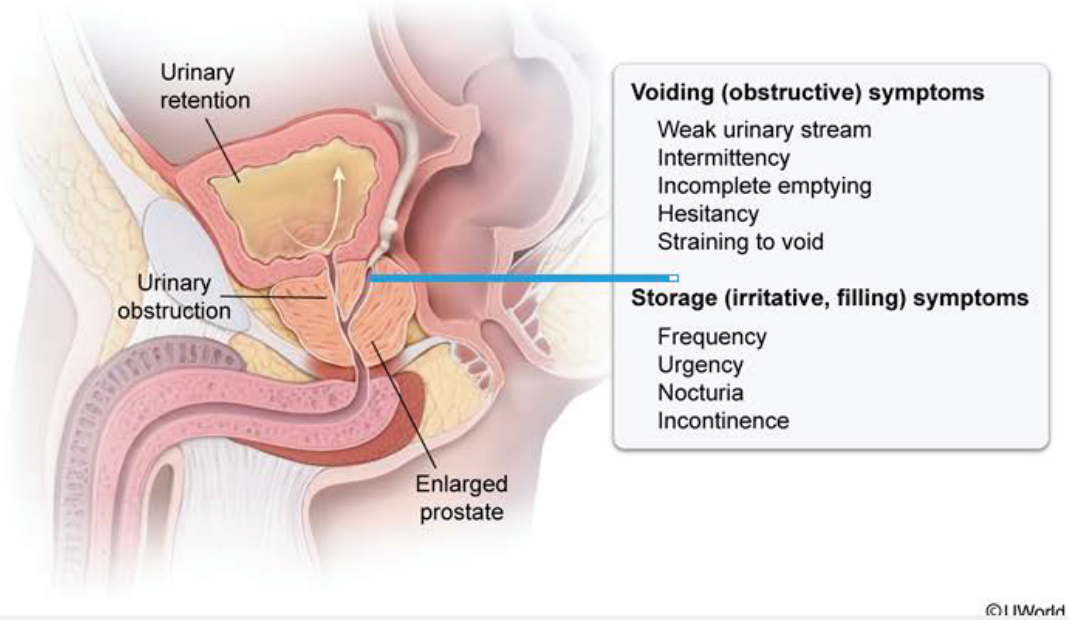
Benign prostatic hyperplasia (BPH)



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of the pelvis on CT scan. Benign prostatic hyperplasia is a common, age-related condition that causes

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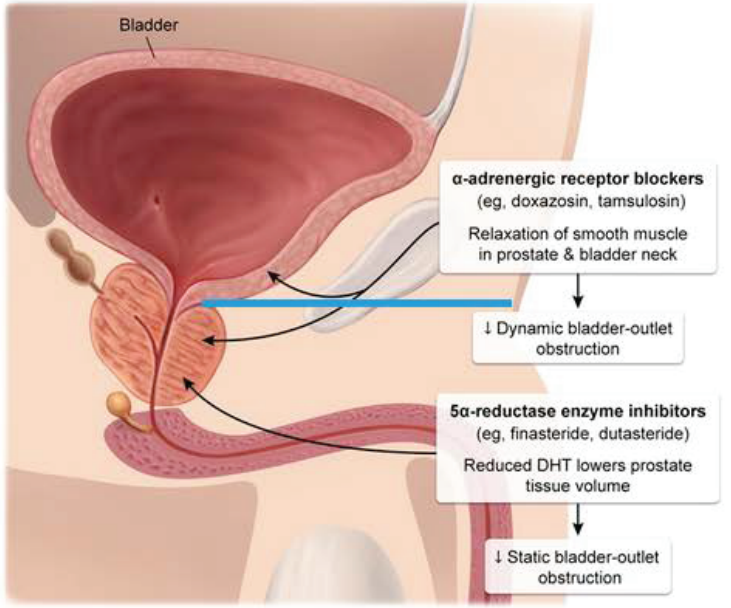
Benign prostatic hyperplasia (BPH)



DHT = dihydrotestosterone.

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of the pelvis on CT scan. Benign prostatic hyperplasia is a common, age-related condition that causes

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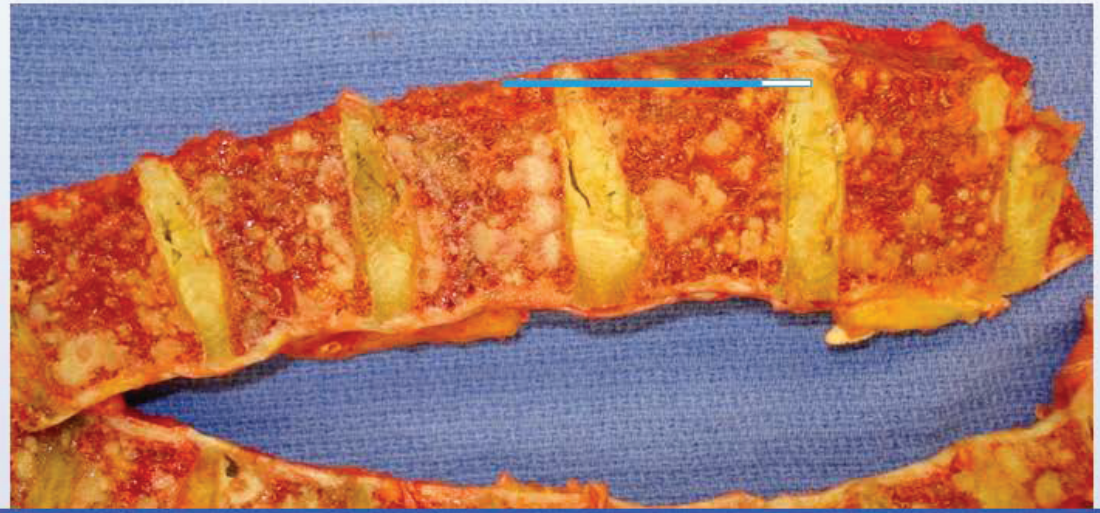
Educational objective:
The prostate is located between the pubic symphysis and the anal canal and is visible on inferior sections of the pelvis on CT scan. Benign prostatic hyperplasia is a common, age-related condition that causes urinary symptoms (eg, hesitancy, straining, incomplete voiding). It can be medically treated with α-adrenergic blockers and 5-α reductase inhibitors.

References

A 77-year-old man is brought to the emergency department due to acute-onset chest pain, shortness of breath, and syncope. Medical history is significant for coronary artery disease, which was treated with right coronary artery stenting 5 years ago. The patient develops cardiac arrest and resuscitation is unsuccessful. Autopsy shows a large bilateral pulmonary embolism occluding the pulmonary trunk. Further history obtained from the patient's wife indicates that he has had constant back pain over the past few months. Autopsy of the vertebrae is shown in the image below:



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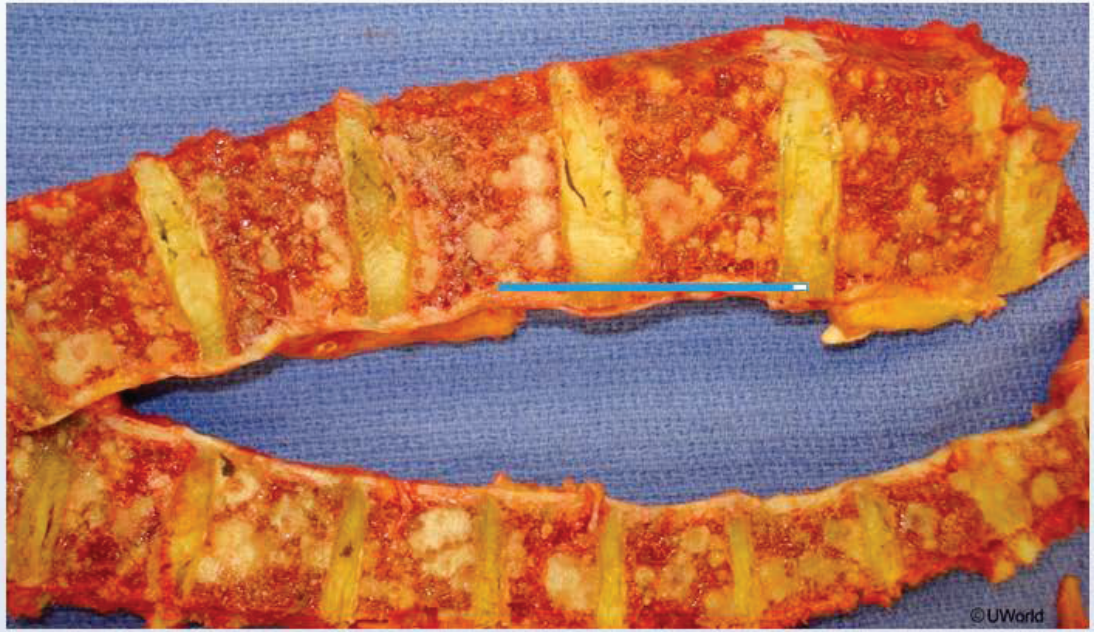
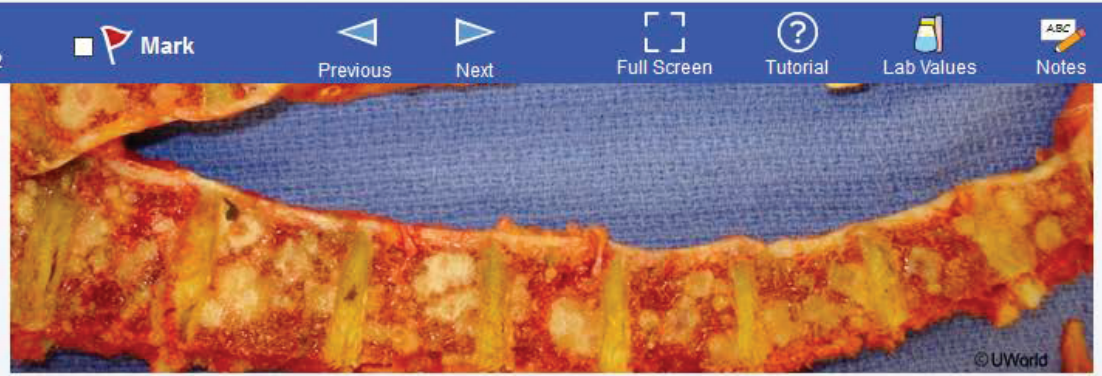


Histologic examination of the bone lesions in this patient would most likely show which of the following?



Histologic examination of the bone lesions in this patient would most likely show which of the following?

A. Aggregates of pleomorphic neoplastic cells containing coarse, brown pigment
B. Cells with enlarged nuclei and prominent nucleoli forming irregular glands
C. Effacement of bone marrow with clusters of plasmablasts and plasma cells
D. Sheets of neoplastic cells with abundant clear cytoplasm
E. Tumor cells showing a complex papillary pattern and psammoma bodies

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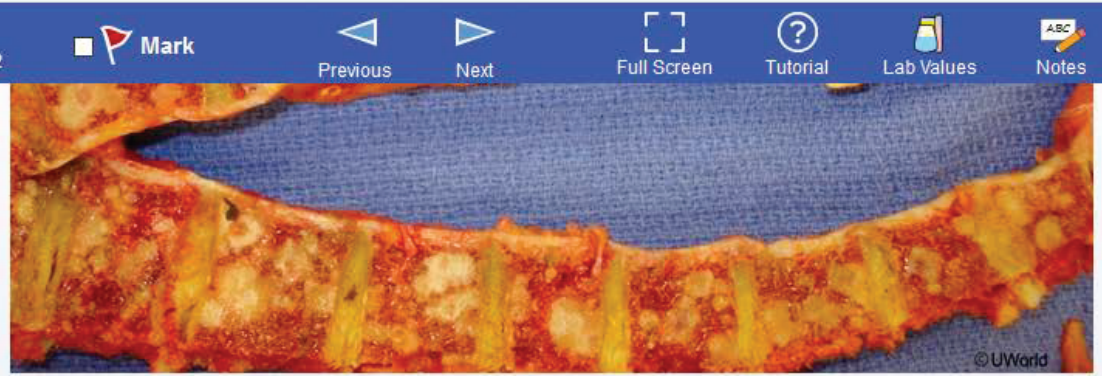

Histologic examination of the bone lesions in this patient would most likely show which of the following?

A. Aggregates of pleomorphic neoplastic cells containing coarse, brown pigment (9%)

✓ B. Cells with enlarged nuclei and prominent nucleoli forming irregular glands (46%)

C. ~~Effacement of bone marrow with clusters of plasmablasts and plasma cells~~ (26%)

D. ~~Sheets of neoplastic cells with abundant clear cytoplasm~~ (12%)

E. Tumor cells showing a complex papillary pattern and psammoma bodies (5%)

Correct

46%
Answered correctly

58 secs
Time Spent

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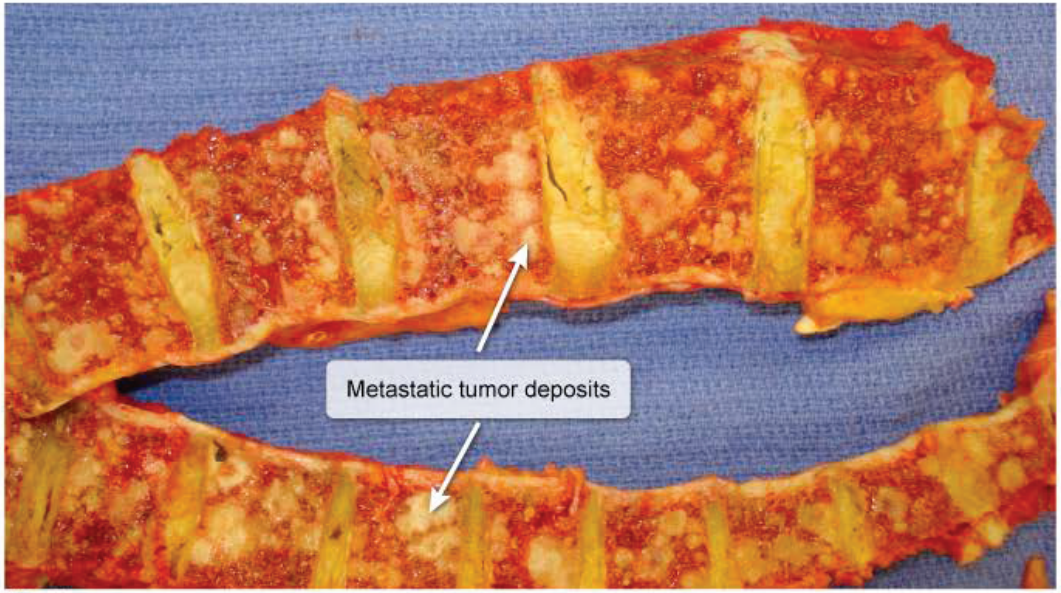
Metastatic prostatic adenocarcinoma to spine



This patient's vertebral body **bony lesions** raise strong suspicion for osteoblastic metastases due to **prostate adenocarcinoma**; his massive pulmonary embolism was likely precipitated by an underlying

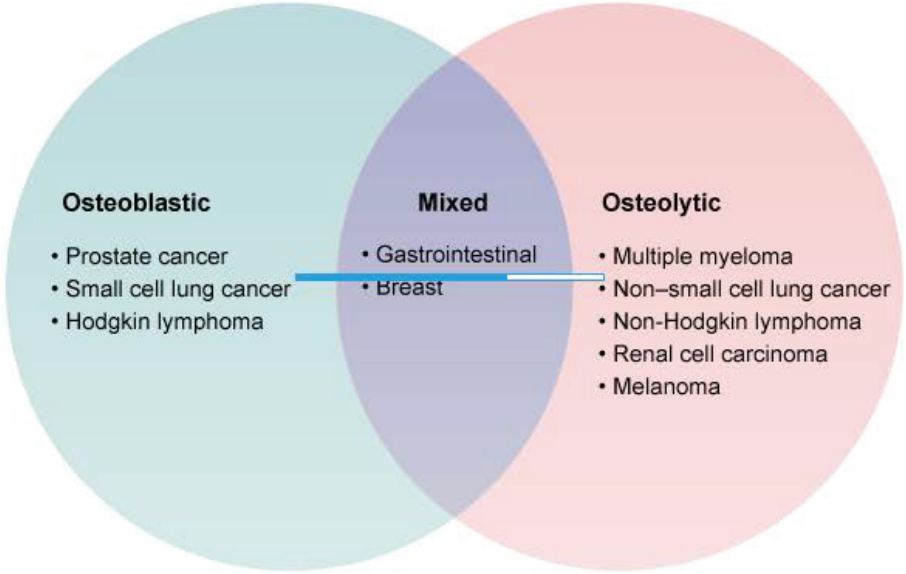
This patient's vertebral body **bony lesions** raise strong suspicion for osteoblastic metastases due to **prostate adenocarcinoma**; his massive pulmonary embolism was likely precipitated by an underlying **hypercoagulable state** of malignancy. Prostate cancer is the most common non-skin cancer in men, and risk is strongly linked to **advancing age**. Because most cases develop in the periphery of the prostate gland, urinary symptoms are uncommon until late in the disease course; therefore, the diagnosis is usually prompted by elevated prostate-specific antigen level, abnormal digital rectal examination, or symptoms related to advanced disease (eg, **bone pain**).

Prostate cancer preferentially metastasizes to **bone** due to specific adhesion molecules (eg, CXCR4) and receptor ligands (eg, RANK) on the cancer cell surface that adhere to pericytes and bone marrow stromal cells. After it establishes a nidus, the tumor secretes **osteoblast differentiation factors** (eg, endothelin 1, insulin-like growth factors, platelet-derived growth factors, bone morphogenic proteins) that promote new bone growth. Biopsy of a bone lesion would most likely show disordered trabecular growth and evidence of prostate cancer cells such as irregular glands with enlarged nuclei and prominent nucleoli.

(Choices A, C, D, and E) *Osteolytic* bone metastases appear on radiology and gross pathology as *moth-eaten* bone, not areas of bony growth. These bone lesions are typically seen with metastatic melanoma (pleomorphic cells with coarse, brown melanin pigment), multiple myeloma (effacement of marrow with

Exhibit Display

Bone metastases



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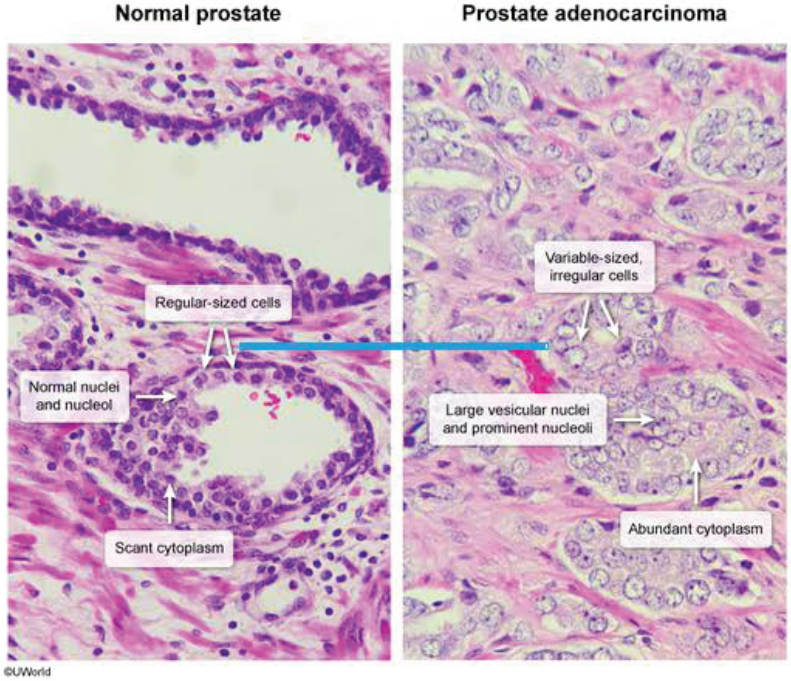

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cells. After it establishes a nidus, the tumor secretes **osteoblast differentiation factors** (eg, endothelin 1, insulin-like growth factors, platelet-derived growth factors, bone morphogenic proteins) that promote new bone growth. Biopsy of a bone lesion would most likely show disordered trabecular growth and evidence of prostate cancer cells such as irregular glands with enlarged nuclei and prominent nucleoli.

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Educational objective:
Prostate cancer is common in older men and metastasizes primarily to bone due to bone-specific tumor adhesion molecules and receptor ligands on the cellular surface. Prostate cancer causes osteoblastic lesions that result in new bone growth. Biopsy would show disordered trabeculae and signs of prostate cancer such as irregular glands with enlarged nuclei and prominent nucleoli.

Pathology	Male Reproductive System	Prostate cancer
Subject	System	Topic

cells. After it establishes a nidus, the tumor secretes **osteoblast differentiation factors** (eg, endothelin 1,

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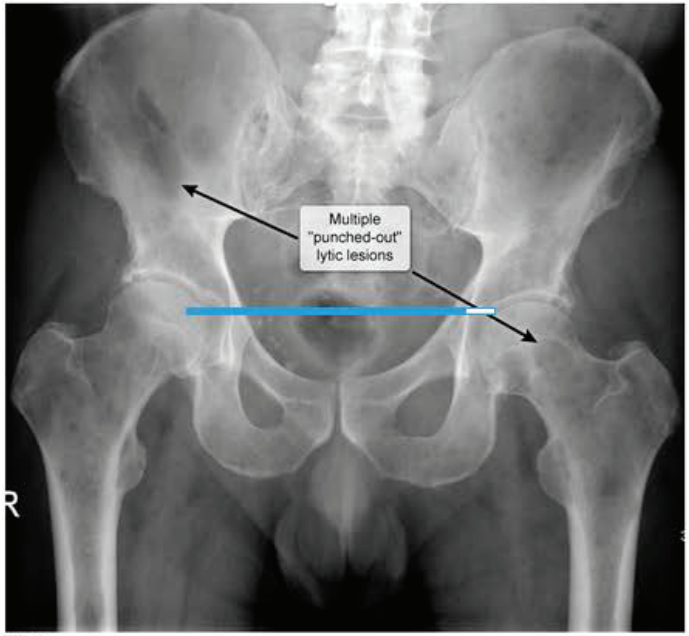
Multiple myeloma



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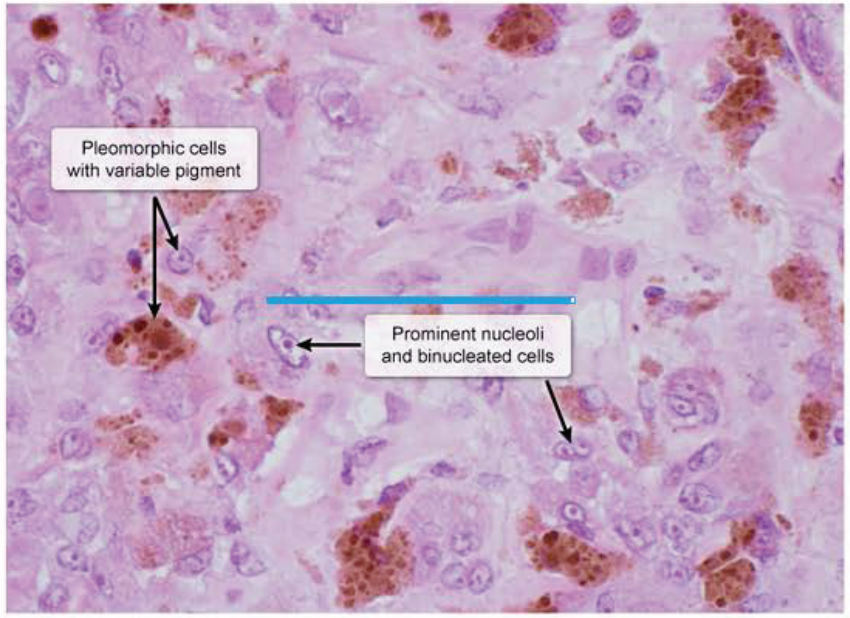
Metastatic melanoma



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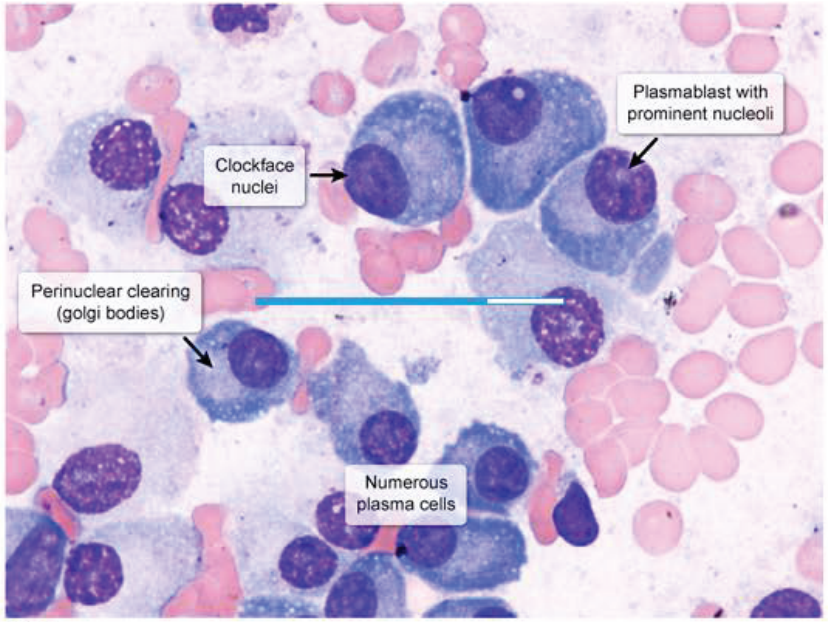
Plasma cell neoplasm (multiple myeloma)



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cells. After it establishes a niduS, the tumor secretes **osteoblast differentiation factors** (eg, endothelin 1,

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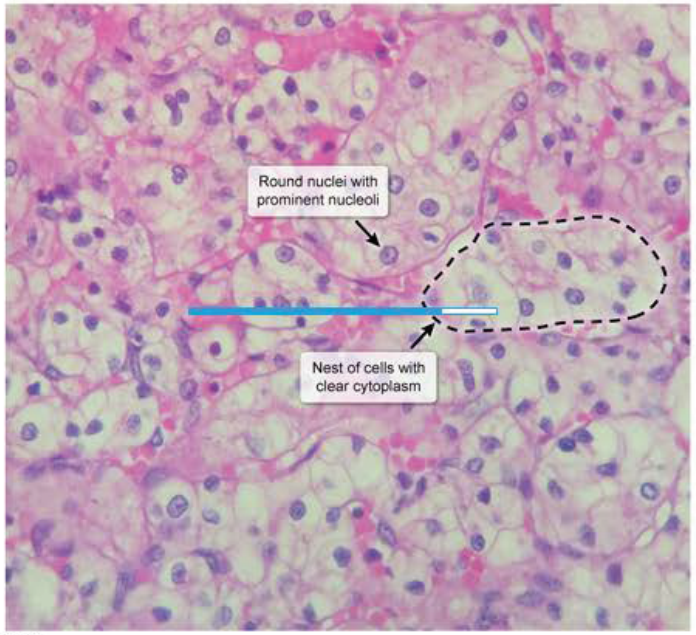
Renal clear cell carcinoma



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cells. After it establishes a nidus, the tumor secretes **osteoblast differentiation factors** (eg, endothelin 1,

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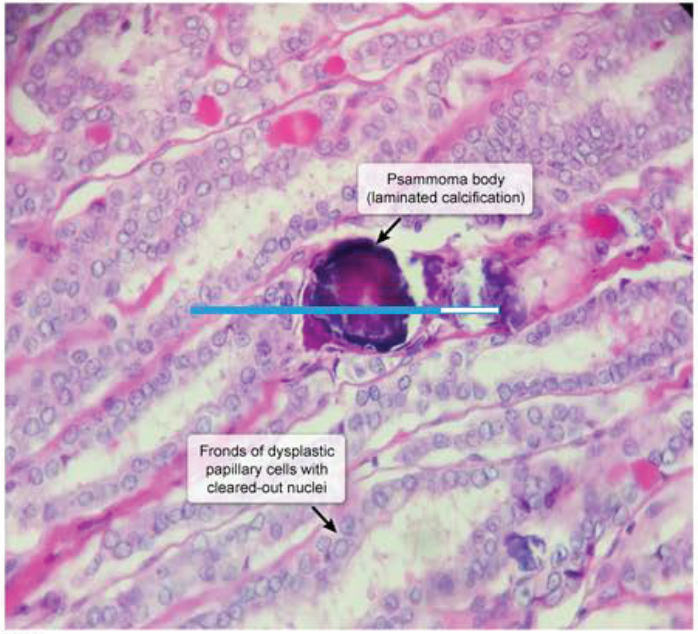
Papillary thyroid carcinoma



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A 66-year-old man comes to the office due to 2 episodes of hematuria over the past month. Digital rectal examination reveals an indurated prostate with no palpable nodules. An image from a transrectal prostate biopsy is shown in the exhibit. Which of the following is the most likely underlying cause of this patient's symptoms?

A. Acute bacterial infection of the prostate
B. Benign hyperplasia of the prostatic stroma
C. Chronic bacterial inflammation of the prostate
D. Invasive carcinoma arising from the urethra
E. Neoplastic proliferation of prostate gland cells

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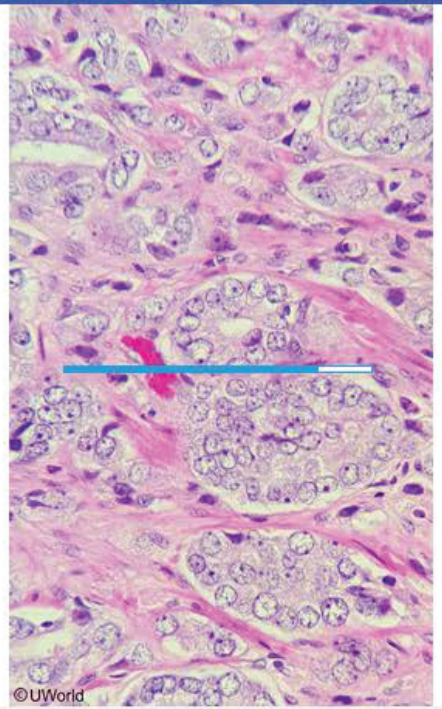

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A. ~~Acute bacterial infection of the prostate~~ (4%)
B. Benign hyperplasia of the prostatic stroma (21%)
C. ~~Chronic bacterial inflammation of the prostate (13%)~~
D. Invasive carcinoma arising from the urethra (9%)
✓ E. Neoplastic proliferation of prostate gland cells (51%)

Correct

51%
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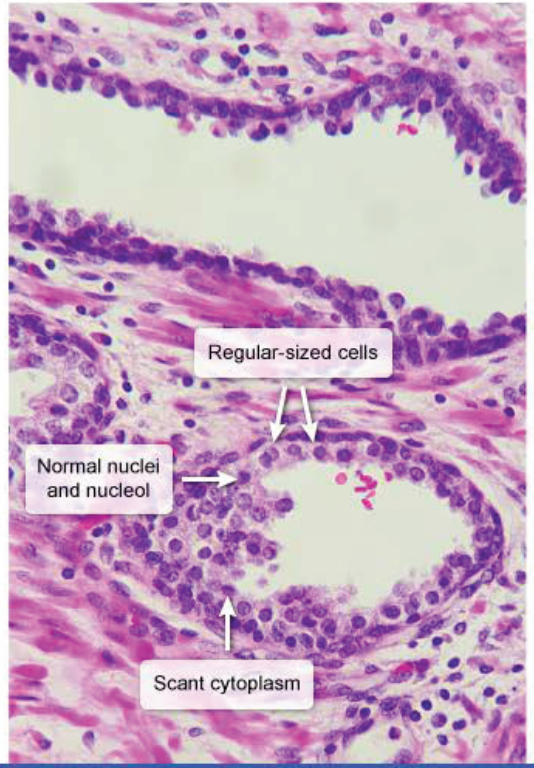
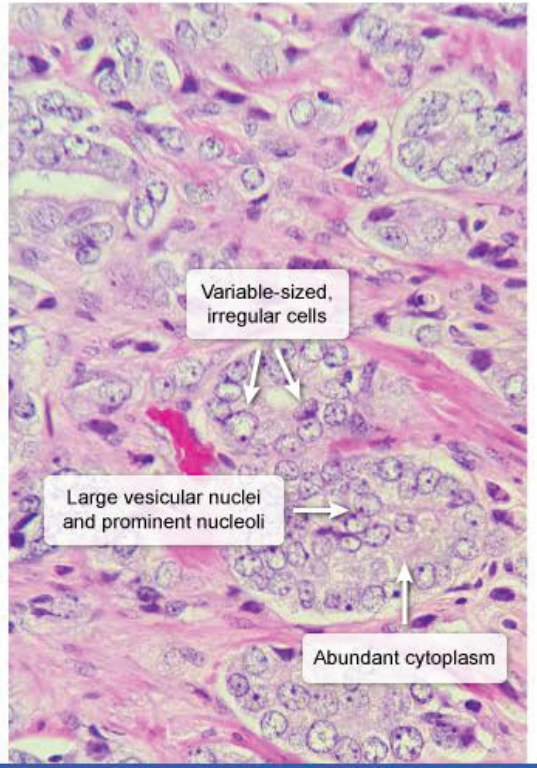
Explanation

Normal prostate



Prostate adenocarcinoma



This older man with an indurated prostate has histopathologic evidence of atypical glandular cells with large nuclei and prominent nucleoli, raising strong suspicion for **prostate adenocarcinoma**. Because most cases of prostate cancer arise in the periphery of the gland (peripheral zone) far from the prostatic portion of the urethra, patients do not typically present with urinary symptoms. However, a minority of cases occur in the portion of the gland (transition zone) that abuts the urethra, which can lead to **hematuria** and/or obstructive voiding manifestations.

Diagnostic evaluation begins with **digital rectal examination**; patients with prostate cancer often have an **indurated** (ie, abnormally firm), nontender gland with or without a nodule. An elevated prostate-specific antigen level adds supporting evidence. Confirmation is typically made by transrectal prostate biopsy, in which 10-12 random core biopsies of the gland are obtained. In contrast to normal prostatic cells, which are small, organized, and glandular, cancer cells typically display varying degrees of cellular atypia, including disorganized or no glandular structure, enlarged nuclei, and prominent nucleoli.

(Choices A and C) Acute prostatitis typically causes systemic symptoms (eg, fever, malaise), dysuria, and a tender, boggy prostate on digital rectal examination. Chronic prostatitis is generally marked by perineal pain and recurrent symptoms of urinary tract infection. Although patients can have hematuria with these conditions, biopsy would show inflammatory, not atypical glandular, cells.

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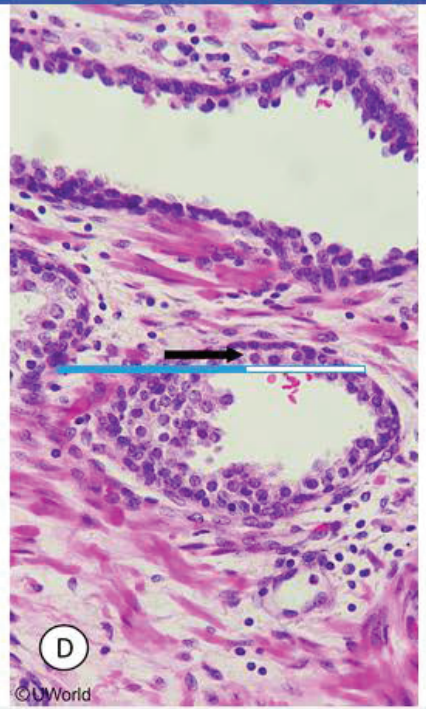

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(Choices A and C) Acute prostatitis typically causes systemic symptoms (eg, fever, malaise), dysuria, and a tender, boggy prostate on digital rectal examination. Chronic prostatitis is generally marked by perineal pain and recurrent symptoms of urinary tract infection. Although patients can have hematuria with these conditions, biopsy would show inflammatory, not atypical glandular, cells.

(Choice B) Benign prostatic hyperplasia is common in older men. Hyperplasia of prostatic stroma in the area of the prostate that surrounds the urethra generally results in voiding symptoms (eg, hesitancy, dribbling, frequency). Hematuria may occasionally occur. Digital rectal examination generally reveals a symmetrically enlarged prostate with no nodules. Biopsy would show extensive stromal hyperplasia, not atypical glands.

(Choice D) Urothelial carcinoma from the bladder or urethra can occasionally invade the prostate. Although this cancer often causes hematuria, biopsy typically shows cancerous uroepithelial cells, not atypical glands. Furthermore, prostate cancer is a far more common cause of an indurated prostate with atypical glandular cells than a urothelial tumor invading the prostate.

Educational objective:
Prostate adenocarcinoma is generally diagnosed with transrectal prostate biopsy, which usually reveals

area of the prostate that surrounds the urethra generally results in voiding symptoms (eg, hesitancy, dribbling, frequency). Hematuria may occasionally occur. Digital rectal examination generally reveals a symmetrically enlarged prostate with no nodules. Biopsy would show extensive stromal hyperplasia, not atypical glands.

(Choice D) Urothelial carcinoma from the bladder or urethra can occasionally invade the prostate. Although this cancer often causes hematuria, biopsy typically shows cancerous uroepithelial cells, not atypical glands. Furthermore, prostate cancer is a far more common cause of an indurated prostate with atypical glandular cells than a urothelial tumor invading the prostate.

Educational objective:
Prostate adenocarcinoma is generally diagnosed with transrectal prostate biopsy, which usually reveals atypical glandular cells with enlarged nuclei and prominent nucleoli. In contrast, normal prostate cells are small and glandular with scant cytoplasm, small nuclei, and normal nucleoli.

Pathology	Male Reproductive System	Prostate cancer
Subject	System	Topic

A 17-year-old boy is brought to the office for evaluation of bilateral breast enlargement. He first noticed it a few months ago and says that it is slightly painful. His parents are concerned that his breasts are gradually becoming more prominent. The patient is in special education classes due to a long-standing history of learning disabilities. His father has type 2 diabetes mellitus and is on dialysis for chronic renal failure. Height is at the 95th percentile, and weight is at the 25th percentile for age and sex. Symmetrical glandular tissue is palpated under both nipple-areolar complexes. His sense of smell is normal, and his testicles are small and firm. Laboratory evaluation would most likely show which of the following findings?

A. Decreased estradiol
B. Increased androstenedione
C. Increased β-hCG
D. Increased creatinine
E. Increased FSH
F. Increased prolactin
G. Prolonged prothrombin time

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A. Decreased estradiol (1%)
B. Increased androstenedione (16%)
C. Increased β-hCG (1%)
D. Increased creatinine (0%)
✓ E. Increased FSH (62%)
F. Increased prolactin (16%)
G. Prolonged prothrombin time (0%)

Klinefelter syndrome	
Pathogenesis	Nondisjunction of the sex chromosomes, resulting in a 47,XXY male
Clinical features	• Primary hypogonadism • Increased long bone length • Gynecomastia • Learning & socialization difficulties
Laboratory findings	• ↓ Testosterone • ↑ LH & FSH (due to loss of feedback inhibition) • ↑ Estradiol

Klinefelter syndrome (KS) is caused by sex chromosome aneuploidy, which most commonly results in a 47,XXY karyotype. These patients typically have atrophied, hyalinized seminiferous tubules (resulting in low inhibin levels) and damaged Leydig cells (resulting in **low testosterone** levels). The lack of feedback inhibition results in **excess gonadotropins** (increased LH and FSH), which in turn **increase estrogen** levels **(Choice A).**

Primary hypogonadism is the cardinal feature. Phenotypic findings include azoospermia, **small/firm**

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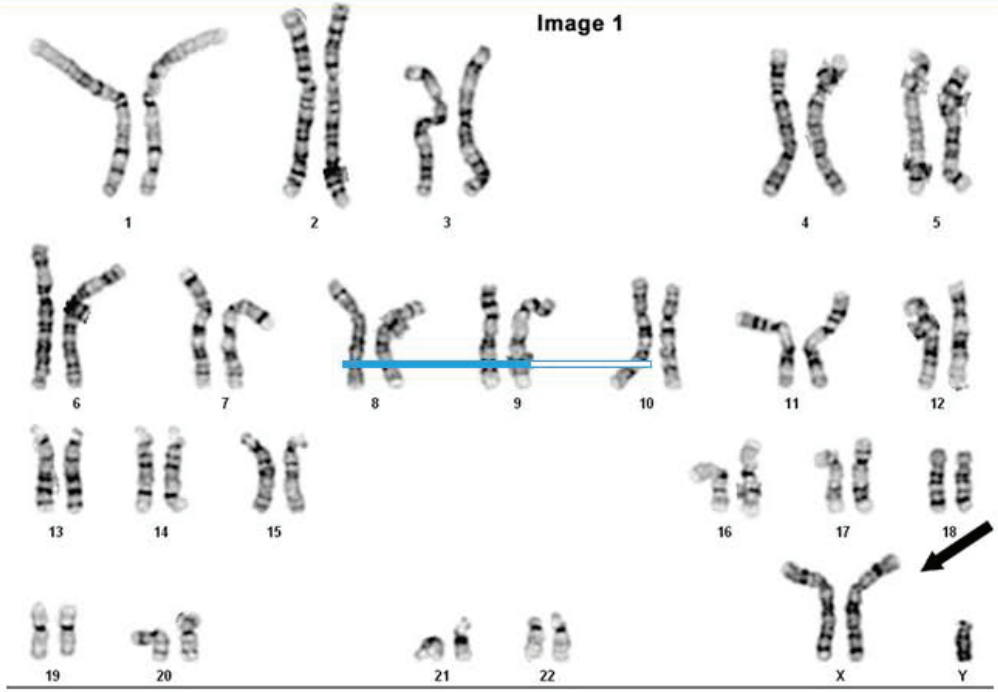

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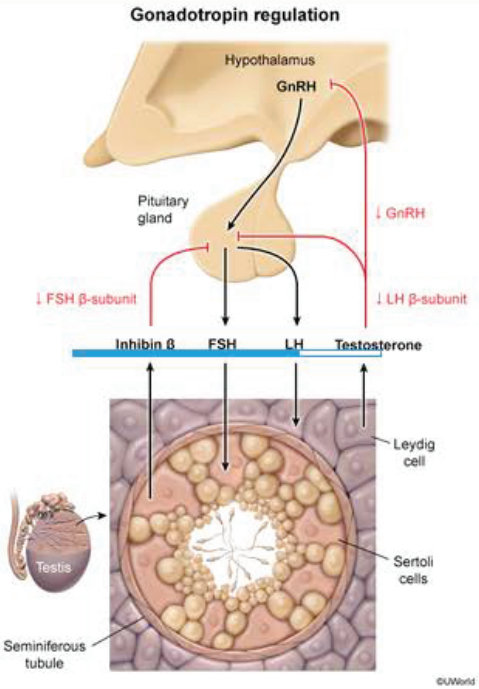

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levels **(Choice A).**

Primary hypogonadism is the cardinal feature. Phenotypic findings include azoospermia, **small/firm testes**, absent secondary male characteristics (including deep voice, beard, and male-pattern pubic hair), and **tall** stature. **Gynecomastia** is also common and associated with a risk of malignant transformation. Cognitive impairment is characterized by learning and socialization difficulties.

(Choice B) Increased androstenedione levels due to anabolic steroid abuse can cause irreversible gynecomastia and testicular atrophy. Exogenous steroid use can be distinguished from KS by the additional findings of acne, male-pattern baldness, hastened epiphyseal closure (reduced height potential), and aggressive behavior.

(Choice C) Testicular germ cell tumors produce excessive β-hCG, resulting in gynecomastia in addition to a firm, rapidly growing testicular mass.

(Choice D) Chronic renal insufficiency is marked by high creatinine and uremia. Uremia is toxic to the testicles and suppresses testosterone production. Renal abnormalities are not a typical feature of KS.

(Choice F) Antipsychotics (eg, haloperidol) can cause hyperprolactinemia, which in turn can induce gynecomastia. Excess prolactin is also secreted from prolactinomas. Prolactin levels are not typically

(Choice D) Chronic renal insufficiency is marked by high creatinine and uremia. Uremia is toxic to the testicles and suppresses testosterone production. Renal abnormalities are not a typical feature of KS.

(Choice F) Antipsychotics (eg, haloperidol) can cause hyperprolactinemia, which in turn can induce gynecomastia. Excess prolactin is also secreted from prolactinomas. Prolactin levels are not typically elevated in other causes of gynecomastia.

(Choice G) Gynecomastia is commonly seen in cirrhosis, particularly in the setting of alcohol abuse. The estrogen-to-testosterone ratio is disrupted due to impaired hepatic degradation of estrogens in addition to ethanol's direct inhibition of testosterone production. Patients with cirrhosis are often coagulopathic due to diminished clotting factor production, which results in increased prothrombin time/International Normalized Ratio.

Educational objective:

Patients with Klinefelter syndrome (47,XXY) have primary hypogonadism characterized by low testosterone and elevated gonadotropin (FSH, LH) levels. In addition, elevated estradiol results in the common finding of gynecomastia.

References

- Klinefelter syndrome: the commonest form of hypogonadism, but often overlooked or untreated.

A 13-year-old boy is brought to the office for a new patient visit. The patient recently immigrated to the United States with his family. He has no history of significant illness, trauma, or surgery. Physical examination shows Tanner stage IV genitalia but an empty right scrotal sac. A round mass can be palpated in the right inguinal canal. Biopsy of the mass shows marked fibrotic changes with prominent Leydig cells and hypoplastic Sertoli cells. The patient's parents are advised that the mass should be removed. Which of the following is the most likely explanation for the need for surgery in this patient?

A. Maintain adequate function of the contralateral organ
B. Preserve virilization
C. Prevent recurrent infections
D. Reduce the risk of future infertility
E. Reduce the risk of malignancy

Submit

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A. Maintain adequate function of the contralateral organ (1%)
B. Preserve virilization (1%)
C. Prevent recurrent infections (1%)
D. Reduce the risk of future infertility (6%)
✓ E. Reduce the risk of malignancy (89%)

Correct

89%
Answered correctly

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10/14/2020
Last Updated

Cryptorchidism	
Clinical features	• Empty scrotum or hemiscrotum • +/− Mass in inguinal canal
Treatment	• Orchiopexy before age 1
Complications	• Decreased fertility • Testicular cancer • Testicular torsion

This patient has an undescended testis, or **cryptorchidism**. Embryologically, the testes originate within the abdomen and then migrate to the scrotal sac via the inguinal canal. The cause of cryptorchidism is poorly understood in most cases. Undescended testes may be unilateral or bilateral and can lie anywhere along the path from the abdomen to the scrotal sac. The temperature inside the scrotal sac is lower than normal body temperature, creating an ideal environment for sperm production. The **seminiferous tubules** and the Sertoli cells within them are very temperature-sensitive and prone to heat-induced damage.

If uncorrected, cryptorchidism leads to atrophy and necrosis of the seminiferous tubules, resulting in **decreased fertility**. Patients with cryptorchidism are at increased risk for **testicular cancer**. Orchiopexy

If uncorrected, cryptorchidism leads to atrophy and necrosis of the seminiferous tubules, resulting in **decreased fertility**. Patients with cryptorchidism are at increased risk for **testicular cancer**. Orchiopexy (moving the testes into the scrotal sac) reduces but does not eliminate the risk of malignancy and is most effective when performed between age 6 months and 1 year.

(Choice A) In unilateral cryptorchidism, the contralateral testis functions normally and is not at increased risk for malignancy or torsion.

(Choice B) Unlike the seminiferous tubules, the testosterone-producing Leydig cells are not very sensitive to temperature. Testosterone levels and virilization are usually normal.

(Choice C) No increased risk for testicular or genitourinary tract infection is found with cryptorchidism.

(Choice D) Orchiopexy before age 1-2 may provide some advantage to future fertility. Beyond age 2, no evidence demonstrates that orchiopexy can preserve sperm count in the undescended testis.

Educational objective:
In undescended testes, the seminiferous tubules atrophy if uncorrected due to higher body temperatures, resulting in decreased fertility and increased risk for malignancy. Orchiopexy (surgical placement of the testes in the scrotal sac) can minimize damage and decrease risk for testicular cancer.

A 28-year-old man comes to the office due to a bump on his right testicle. The patient is otherwise asymptomatic and healthy. Vital signs are normal. A solid mass is palpated in the right testicle. The rest of the examination is unremarkable. A scrotal ultrasound reveals a suspicious, partially necrotic mass. Serum lactate dehydrogenase and alpha-fetoprotein levels are markedly elevated. The patient undergoes a right radical inguinal orchiectomy. Which of the following is the most likely histologic diagnosis?

A. Leydig cell tumor
B. Nonseminomatous germ cell tumor
C. Sertoli cell tumor
D. Teratoma
E. Testicular lymphoma

Submit

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A. ~~Leydig cell tumor~~ (4%)

✓ B. Nonseminomatous germ cell tumor (79%)

C. ~~Sertoli cell tumor~~ (6%)

D. Teratoma (9%)

E. Testicular lymphoma (1%)

Correct

79%
Answered correctly

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Testicular cancer	
Epidemiology	• Age 15-35 • Risk factors: family history, cryptorchidism
Types	• Germ cell tumors (95%): seminomatous or nonseminomatous (embryonal carcinoma, yolk sac, choriocarcinoma, teratoma, mixed) • Sex cord–stromal tumors: Sertoli cell, Leydig cell
Manifestations	• Unilateral, painless testicular mass • Dull ache in lower abdomen
Diagnosis	• Examination: firm, ovoid mass • Elevated tumor markers (AFP, β-hCG, LDH) • Scrotal ultrasound

AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

This patient's painless testicular lesion, necrotic mass on ultrasound, and elevated serum alpha-fetoprotein (AFP) level raises strong suspicion for **testicular cancer**, the most common solid organ malignancy in men

AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

This patient's painless testicular lesion, necrotic mass on ultrasound, and elevated serum alpha-fetoprotein (AFP) level raises strong suspicion for **testicular cancer**, the most common solid organ malignancy in men age 15-35. Most cases (>95%) arise from pluripotent germ cells that normally differentiate into sperm (**germ-cell tumors**), which are categorized as follows:

- **Non-seminomatous germ cell tumors** (NSGCT) contain undifferentiated or partially differentiated germ cells (eg, embryonal carcinoma, yolk sac tumor, choriocarcinoma). They often generate abnormal hormones (human chorionic growth [**hCG**] hormone) or proteins (**AFP**) that can be measured in the blood to aid diagnosis and evaluate for recurrence following treatment.
- Seminomas contain large uniform germ cells that retain the phenotypic features of spermatogonia. They do not produce AFP but some seminomas secrete limited quantities of hCG.

Lactate dehydrogenase (LDH), a marker of tissue injury and cell turnover, is also often elevated in patients with germ cell tumors but is less sensitive and specific than hCG or AFP.

(Choice A) Leydig cells secrete testosterone and are found in the testicular stroma. Leydig cell tumors often produce estrogen or testosterone, leading to feminization (eg, gynecomastia) or precocious puberty, respectively. They do not generate AFP or hCG.

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(Choice C) Sertoli cells nourish sperm and secrete inhibin, which moderates pituitary gonadotropin release. Sertoli cell tumors are sometimes associated with the excessive production of estrogen but do not typically elevate AFP.

(Choice D) Teratomas are terminally differentiated germ cells that may contain skin or gastrointestinal epithelium, cartilage, and/or neuronal tissue. They are often malignant in adults and may be part of some nonseminomatous germ cell tumors. However, terminally differentiated cells are not generally able to produce AFP or hCG; therefore, these tumor markers are usually not elevated.

(Choice E) Primary testicular lymphoma is uncommon and usually occurs in men age >60. Although lymphoma can be associated with elevated LDH, AFP is almost always normal.

Educational objective:
Most cases of testicular cancer are either seminomatous or nonseminomatous germ cell tumors. Nonseminomatous germ cell tumors are composed of partially differentiated germ cells, which often retain the ability to secrete human chorionic growth hormone and alpha-fetoprotein (serum tumor markers).

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An 18-year-old man comes to the office due to a mass in his left scrotum. He has no other symptoms. The patient plays basketball regularly but does not recall any recent trauma to the testicle. He is sexually active with 2 partners and does not use condoms. Vital signs are within normal limits. Physical examination shows a left intrascrotal nodule that is difficult to distinguish from the left testis. The mass is nontender, does not change in size upon supine positioning, and does not transilluminate. There is no inguinal lymphadenopathy. Which of the following is the most likely diagnosis?

A. Epididymitis
B. Hydrocele
C. Syphilitic gumma
D. Testicular cancer
E. Testicular hematoma
F. Varicocele

Submit

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A. ~~Epididymitis~~ (13%)
B. ~~Hydrocele~~ (0%)
C. Syphilitic gumma (7%)
✓ D. Testicular cancer (64%)
E. ~~Testicular hematoma~~ (6%)
F. ~~Varicocele~~ (7%)

Testicular cancer	
Epidemiology	• Age 15-35 • Risk factors: family history, cryptorchidism
Types	• Germ cell tumors (95%): seminomatous or nonseminomatous (embryonal carcinoma, yolk sac, choriocarcinoma, teratoma, mixed) • Sex cord–stromal tumors: Sertoli cell, Leydig cell
Manifestations	• Unilateral, painless testicular mass • Dull ache in lower abdomen
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AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

The presence of a **painless, solid testicular mass** should always be considered **testicular cancer** until

AFP = alpha-fetoprotein; **LDH** = lactate dehydrogenase.

The presence of a **painless, solid testicular mass** should always be considered **testicular cancer** until proven otherwise. Most cases present with a nodule or solid swelling in one testicle, which is often initially noticed by a partner or after a minor trauma. Bimanual examination of scrotal contents generally reveals a firm, hard, or fixed **nodule** within the tunica albuginea (fibrous covering of testes) that is ovoid in shape and painless to palpation. Because light does not penetrate solid tumors, testicular cancer does not transilluminate (unlike fluid-filled hydroceles) **(Choice B)**. Bilateral scrotal ultrasound and serum tumor markers (eg, alpha-fetoprotein, beta human chorionic growth hormone) are usually obtained next to aid diagnosis.

Most testicular tumors arise in young men (age 15-35) and are derived from a pluripotent testicular germ cell; these testicular **germ cell tumors** are generally curable with surgery and (when needed) chemotherapy.

(Choice A) Epididymitis is common in young, sexually active men and is usually due to a sexually transmitted infection (eg, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*). However, most cases are quite painful, and careful examination usually shows swelling adjacent to, rather than within, the testis.

(Choice C) Syphilitic gummas are a manifestation of tertiary syphilis that can develop many years after

transmitted infection (eg, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*). However, most cases are quite painful, and careful examination usually shows swelling adjacent to, rather than within, the testis.

(Choice C) Syphilitic gummas are a manifestation of tertiary syphilis that can develop many years after initial infection in untreated patients. They generally present with painless, white-gray lesions on the skin that may ulcerate; testicular gummas (syphilitic orchitis) are rare and usually associated with pain and fever.

(Choice E) Testicular hematoma usually occurs after scrotal trauma and generally presents with significant testicular pain and tenderness to palpation.

(Choice F) Varicoceles are due to venous dilation in the pampiniform plexus. They can present with painless testicular swelling but characteristically feel like a "bag of worms" on physical examination. Most decompress with recumbency and grow in size with standing.

Educational objective:
A painless, solid scrotal mass should be considered testicular cancer until proven otherwise. Examination generally reveals a solid, firm, or fixed nodule in the tunica albuginea that is ovoid in shape and painless to palpation. Testicular tumors do not transilluminate.

A 45-year-old man comes to the office due to fatigue, lack of sexual desire, and inability to maintain an erection. A year ago, he was advised to lose weight with diet and exercise due to mildly elevated fasting glucose levels. The patient has smoked a pack of cigarettes daily for the past 20 years and drinks an alcoholic beverage 3-4 times per month. Blood pressure is 110/70 mm Hg and pulse is 65/min. Oxygen saturation is 99% on room air. BMI is 29 kg/m^2. Skin examination shows increased pigmentation over the knuckles and face. The liver is palpable 3-4 cm below the right costal margin. The remainder of the examination reveals small testes. Which of the following is most likely contributing to the development of the patient's symptoms?

A. Aortoiliac atherosclerosis
B. Autoimmune adrenalitis
C. Ectopic ACTH production
D. Fibrosis of the seminiferous tubules
E. Iron deposition in the pituitary gland

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erection. A year ago, he was advised to lose weight with diet and exercise due to mildly elevated fasting glucose levels. The patient has smoked a pack of cigarettes daily for the past 20 years and drinks an alcoholic beverage 3-4 times per month. Blood pressure is 110/70 mm Hg and pulse is 65/min. Oxygen saturation is 99% on room air. BMI is 29 kg/m^2. Skin examination shows increased pigmentation over the knuckles and face. The liver is palpable 3-4 cm below the right costal margin. The remainder of the examination reveals small testes. Which of the following is most likely contributing to the development of the patient's symptoms?

A. Aortoiliac atherosclerosis (3%)
B. Autoimmune adrenalitis (17%)
C. Ectopic ACTH production (24%)
D. Fibrosis of the seminiferous tubules (5%)
E. Iron deposition in the pituitary gland (49%)

Correct

49%
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Clinical manifestations of hereditary hemochromatosis	
Skin	• Hyperpigmentation
Musculoskeletal	• Arthritis (particularly 2nd & 3rd MCP joints) • Chondrocalcinosis
Gastrointestinal	• Elevated liver enzymes, hepatomegaly (early) • Cirrhosis & hepatocellular carcinoma (late)
Endocrine	• Diabetes mellitus • Hypopituitarism (eg, secondary hypogonadism, hypothyroidism)
Cardiac	• Restrictive or dilated cardiomyopathy • Conduction abnormalities

MCP = metacarpophalangeal.

This patient's decreased libido, erectile dysfunction, and testicular atrophy are indicative of **hypogonadism**. These findings, in combination with **hyperpigmentation** of the skin, **elevated glucose**/diabetes mellitus, and **hepatomegaly**, are strongly suggestive of **hereditary hemochromatosis**

This patient's decreased libido, erectile dysfunction, and testicular atrophy are indicative of **hypogonadism**. These findings, in combination with **hyperpigmentation** of the skin, **elevated glucose**/diabetes mellitus, and **hepatomegaly**, are strongly suggestive of **hereditary hemochromatosis** (HH).

HH is an autosomal recessive disorder characterized by excessive intestinal iron absorption and accumulation in various tissues. **Secondary hypogonadism** occurs in HH due to **deposition of iron in the pituitary gland**, resulting in decreased gonadotropin secretion and subsequent testicular failure. In women, HH is often not diagnosed until after menopause, as premenopausal women have ongoing menstrual blood loss that usually prevents significant iron overload and symptom development; therefore, amenorrhea is a rare finding in women with HH.

(Choice A) Atherosclerotic disease is a common cause of erectile dysfunction in older men, especially those with a history of smoking, but it typically would not affect libido and would not cause hyperpigmentation or hepatomegaly.

(Choice B) Autoimmune adrenalitis is a common cause of primary adrenal insufficiency (ie, Addison disease). Hyperpigmentation is common due to increased cosecretion of melanocyte-stimulating hormone with ACTH, but patients typically have orthostatic hypotension (due to loss of mineralocorticoid) and

(Choice B) Autoimmune adrenalitis is a common cause of primary adrenal insufficiency (ie, Addison disease). Hyperpigmentation is common due to increased cosecretion of melanocyte-stimulating hormone with ACTH, but patients typically have orthostatic hypotension (due to loss of mineralocorticoid) and hypoglycemia (not hyperglycemia).

(Choice C) Ectopic ACTH secretion causes paraneoplastic Cushing syndrome (eg, small cell lung cancer). Patients may develop hyperpigmentation and hyperglycemia but also often have hypertension and proximal muscle weakness. Small testes are not seen.

(Choice D) Testicular fibrosis is a common manifestation of Klinefelter syndrome (KS). Hypogonadism due to KS is typically apparent at puberty and is often associated with a eunuchoid habitus, sparse body hair, and high-pitched voice. Hepatomegaly is not common.

Educational objective:
Hereditary hemochromatosis can cause secondary hypogonadism due to deposition of iron in the pituitary gland, resulting in decreased gonadotropin secretion. Patients who develop secondary hypogonadism are also at risk for deficiencies in other pituitary hormones (eg, central hypothyroidism).

Pathology	Male Reproductive System	Hemochromatosis
Subject	System	Topic

A 62-year-old man comes to the office due to an elevated prostate-specific antigen level on a screening test. When asked about genitourinary symptoms, the patient says, "It often takes a bit of time before my urine starts flowing," but he has no other problems. Abdominal and external genital examinations are unremarkable. Digital rectal examination reveals hard prostate nodules. A biopsy confirms adenocarcinoma, and the patient undergoes a radical prostatectomy. During the surgery, the nerves within the fascia surrounding the gland are inadvertently injured. Which of the following is the most likely consequence of the nerve injury?

A. Detrusor muscle overactivity
B. Erectile dysfunction
C. External urethral sphincter paralysis
D. Fecal incontinence
E. Loss of cremasteric reflex
F. Loss of penile skin sensation

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A. Detrusor muscle overactivity (5%)
B. Erectile dysfunction (57%)
C. External urethral sphincter paralysis (16%)
D. Fecal incontinence (6%)
E. Loss of cremasteric reflex (8%)
F. Loss of penile skin sensation (4%)

Correct

57%
Answered correctly

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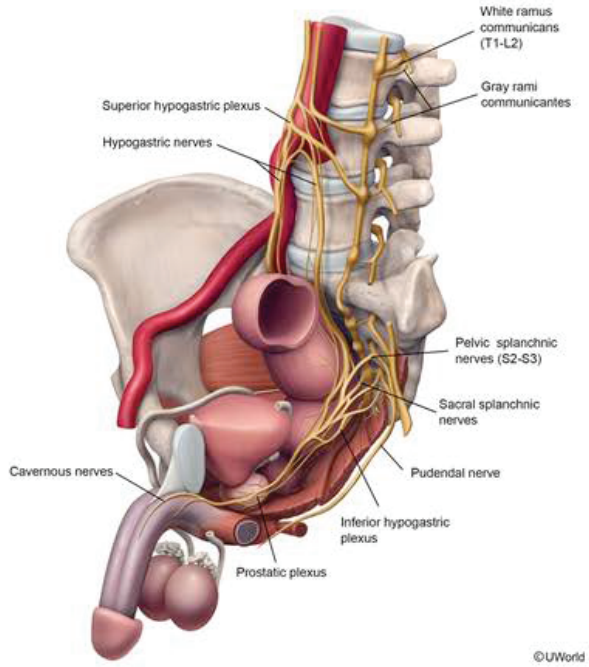
Pelvic autonomic nerves



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The **prostatic plexus** lies within the fascia of the prostate and originates from the **inferior hypogastric plexus** (which itself is a continuation of the hypogastric nerve with additional input from the **pelvic and sacral splanchnic nerves**). The lesser and greater **cavernous nerves** arise from the prostatic plexus and pass beneath the pubic arch to innervate the corpora cavernosa of the penis and urethra. The cavernous nerves carry post-ganglionic parasympathetic fibers that facilitate penile erection. **Prostatectomy** or injury to the prostatic plexus can cause **erectile dysfunction**; as a result, surgeons attempt to preserve the integrity of the prostatic fascial shell during surgery.

(Choice A) Detrusor muscle overactivity leads to urge incontinence, which is more common in women. The detrusor muscle is controlled by parasympathetic fibers from the pelvic splanchnic nerves and inferior hypogastric plexus, which are not usually injured during prostatectomy.

(Choices C, D, and F) Branches of the pudendal nerve innervate the external urethral and anal sphincters. They also provide sensory innervation of the external genitalia. Pudendal nerve injury can lead to fecal incontinence, decreased penile sensation, or external urethral sphincter paralysis. Although urethral muscle injury can occur during prostate surgery, injury to the main pudendal nerve is less common with prostatectomy.

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(Choice E) The cremasteric reflex is elicited by lightly stroking the medial thigh, which causes contraction of the cremaster muscle to pull up the ipsilateral testis. This reflex is mediated by the genitofemoral nerve, which originates from the L1-L2 spinal nerves. Loss of the cremasteric reflex is most commonly seen with testicular torsion or L1-L2 spinal injury.

Educational objective:

The prostatic plexus (inferior hypogastric nerves plus pelvic and sacral splanchnic nerves) lies within the fascia of the prostate and innervates the corpus cavernosa of the penis, which facilitates penile erection. As a result, prostatectomy or injury to the prostatic plexus can cause erectile dysfunction.

References

- Optimizing postoperative sexual function after radical prostatectomy.

Anatomy	Male Reproductive System	Male sexual dysfunction
Subject	System	Topic

A 68-year-old man comes to the office for follow-up. The patient underwent radical prostatectomy for prostate adenocarcinoma 6 months ago, which decreased his serum prostate-specific antigen (PSA) level from 16 ng/mL at the time of surgery to 1 ng/mL 6 weeks after surgery. Initial staging evaluation revealed no evidence of metastatic disease. PSA level is now 8 ng/dL, and repeat imaging reveals regional lymphadenopathy. The patient is prescribed combination therapy with buserelin and bicalutamide. Which of the following is the main reason for adding bicalutamide to this patient's treatment regimen?

A. To block androgen production from adrenal glands
B. To induce apoptotic death of cancer cells
C. To prevent sexual dysfunction from buserelin therapy
D. To prevent testosterone surge effect from buserelin therapy
E. To prevent vasomotor symptoms from buserelin therapy

Submit

A 68-year-old man comes to the office for follow-up. The patient underwent radical prostatectomy for prostate adenocarcinoma 6 months ago, which decreased his serum prostate-specific antigen (PSA) level from 16 ng/mL at the time of surgery to 1 ng/mL 6 weeks after surgery. Initial staging evaluation revealed no evidence of metastatic disease. PSA level is now 8 ng/dL, and repeat imaging reveals regional lymphadenopathy. The patient is prescribed combination therapy with buserelin and bicalutamide. Which of the following is the main reason for adding bicalutamide to this patient's treatment regimen?

A. To block androgen production from adrenal glands (19%)
B. To induce apoptotic death of cancer cells (5%)
C. To prevent sexual dysfunction from buserelin therapy (5%)
✓ D. To prevent testosterone surge effect from buserelin therapy (60%)
E. To prevent vasomotor symptoms from buserelin therapy (9%)

Correct

60%
Answered correctly

44 secs
Time Spent

10/15/2020
Last Updated

Prostate cancer is an **androgen-dependent** tumor early in the disease course. Because androgens in men are primarily made in the testes, patients with recurrent (eg, rising prostate-specific antigen level after prostatectomy) or disseminated (eg, regional lymphadenopathy) prostate cancer are generally treated with surgical or **medical orchiectomy** to reduce systemic androgen levels, thereby reducing the primary growth factor for the tumor.

Androgen production in men is controlled by the hypothalamic-pituitary-testicular axis. **GnRH** is secreted by the hypothalamus in a **pulsatile** fashion, which stimulates pituitary gonadotrophs to release luteinizing hormone (LH); LH then stimulates the Leydig cells of the testes to generate and **secrete androgens**. Patients who undergo medical orchiectomy are often treated with a GnRH analogue (eg, **buserelin**), which stimulates the pituitary gland in a **continuous** fashion, leading to a down-regulation of the GnRH receptor. This subsequently drops LH secretion, which **lowers androgen production** by the testes.

However, because GnRH analogues **temporarily activate** the GnRH receptor prior to downregulation, patients often develop a **surge in androgens** during the first few weeks of therapy. Therefore, androgen-receptor inhibitors (eg, **bicalutamide**) are usually concurrently administered during the first weeks of GnRH analogue therapy to block the activity of androgens on the tumor cells.

(Choice A) Although adrenal synthesis of androgens is not an initial target in prostate cancer, patients who

analogue therapy to block the activity of androgens on the tumor cells.

(Choice A) Although adrenal synthesis of androgens is not an initial target in prostate cancer, patients who have progressive disease despite medical or surgical orchiectomy are often treated with abiraterone, which limits androgen production in the tumor, adrenal gland, and testes by inhibiting the enzyme 17alpha-hydroxylase.

(Choice B) Chemotherapy is often administered with GnRH analogues in patients with metastatic prostate cancer to induce cancer cell death. However, bicalutamide is an androgen-receptor inhibitor, not a chemotherapy agent.

(Choice C) Sexual dysfunction occurs in the majority of men given GnRH analogues due to reduced libido and erectile dysfunction. This can be managed with phosphodiesterase inhibitors.

(Choice E) GnRH analogues often cause vasomotor symptoms (hot flashes) due to estrogen withdrawal. Treatment is similar to menopausal hot flashes in women; progesterone, cyproterone, and selective serotonin reuptake inhibitors are somewhat effective.

Educational objective:
Because prostate cancer is an androgen-dependent tumor, patients with advanced disease are generally treated with surgical or medical orchiectomy. Medical orchiectomy uses GnRH analogues to reduce LH

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Educational objective:
Because prostate cancer is an androgen-dependent tumor, patients with advanced disease are generally treated with surgical or medical orchiectomy. Medical orchiectomy uses GnRH analogues to reduce LH production, which subsequently reduces androgen production in the testes. Because there is an initial surge in androgens at the start of therapy (due to stimulation of the GnRH receptor), patients prescribed GnRH therapy are usually treated with a few weeks of androgen-receptor inhibitors (eg, bicalutamide).

Pharmacology	Male Reproductive System	Prostate cancer
Subject	System	Topic